TAS OS OF ZSIS

Adherence to the Norwegian food-based dietary guidelines indices and the World Cancer Research Fund/American Institute for Cancer Research index in two Norwegian populations

A cross-sectional subproject of the CRC-NORDIET study and the VISA study

Master's Thesis by Agnes Guttormsen

Department of Nutrition Faculty of Medicine University of Oslo

May 2021

Adherence to the Norwegian food-based dietary guidelines indices and the World Cancer Research Fund/American Institute for Cancer Research index in two Norwegian populations

A cross-sectional subproject of the CRC-NORDIET study and the VISA study

By Agnes Guttormsen



Supervisors: Hege Berg Henriksen Karianne Svendsen Rune Blomhoff

Department of Nutrition, Faculty of Medicine UNIVERSITY OF OSLO

May 2021

© Agnes Guttormsen

2021

Adherence to the Norwegian food-based dietary guidelines indices and the World Cancer Research Fund/American Institute for Cancer Research index in two Norwegian populations

Agnes Guttormsen

http://www.duo.uio.no/

Print: Reprosentralen, University of Oslo

Acknowledgements

This master's thesis was conducted at the Department of Nutrition, Faculty of Medicine, University of Oslo, Norway, from August 2020 to May 2021.

First of all, I would like to thank my main supervisor during this year, Dr. Hege Berg Henriksen, for all your support, wide knowledge, encouragement and availability. Thank you for your time, help and guidance through this entire year, I am so grateful! I would also like to express my gratitude to my co-supervisors Dr. Karianne Svendsen, for your engagement, support and positive feedback, and Professor Rune Blomhoff, for your valuable and constructive feedback and support. To clinical dietitian Hedda Beate Berg, I am thankful for all help, proofreading, engagement and support. I want to thank all members of the CRC-NORDIET research group, for including me in your group, for sharing your wide knowledge and for engaging in my thesis. I really appreciate it! To my fellow master students in the CRC-NORDIET study this year; Astrid, Åshild and Sigrid, thank you for your care and support.

Thank you Esther Bergine Bjuland Soteland and Miriam Gustad, for all talks, laughter and coffee breaks, your unlimited support and for always motivating me. This year would not have been the same without you! I would also like to thank all my classmates through these years. We made it! I wish you all the best.

To my dear parents Lise and Alf Inge, my sister; Elisabeth and my brother; Torstein, thank you for encouraging me through all these years, and especially this past year. I really appreciate your endless love and support. To my roomies Hanna and Astrid, and to my friends, thanks for taking care of me, cheering me on and for brightening my days. You are irreplaceable.

Oslo, May 2021

Agnes Guttormsen

Abstract

Background: Adherence to a dietary or lifestyle pattern can be assessed by the use of indices. An index based on the cancer prevention recommendations from the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) has been developed and established, and two indices based on the Norwegian food-based dietary guidelines (NFBDG) have recently been developed, but have not been tested and implemented. **Objectives:** The primary aim was to investigate the adherence to the NFBDG indices and the WCRF/AICR index in a population of colorectal cancer patients and in a population of healthy individuals with moderately elevated risk of cardiovascular disease. Secondary aims included investigation of adherence to the components in the indices, study gender differences in adherence to the indices, and to investigate associations between adherence to the indices and clinical factors (i.e. blood pressure (BP), plasma lipids, and body mass index (BMI)). Methods: This cross-sectional study included 494 participants of the ongoing CRC-NORDIET study and 381 participants of the VISA study. Adherence to the NFBDG indices and the WCRF/AICR index in the two populations was assessed at baseline of each study, using semi-quantitative food frequency questionnaires and anthropometric measurements. Results: In the CRC-NORDIET population, mean adherences were 45 %, 52 %, and 57 % in the NFBDG diet index, the WCRF/AICR index and the NFBDG lifestyle index, respectively. The mean adherences in the VISA population were 46 %, 53 %, and 61 % in the NFBDG diet index, the WCRF/AICR index and the NFBDG lifestyle index, respectively. The participants in both populations had highest adherence to the recommendations on whole grains, fish, sugar-sweetened beverages, physical activity and tobacco, and lowest adherence to the recommendations on red and processed meat, foods high in sugar and fat, and unsalted nuts. Compared to men, women had significantly higher adherence to all indices in both study populations (p<0.05), except for the NFBDG lifestyle index in the VISA population. Inverse associations were found between adherence to an index and diastolic BP, triglycerides, and BMI (p<0.05), but this was inconclusive across the three indices and in the two populations. Conclusion: Most participants in both study populations were moderate adherent to the two NFBDG indices and the WCRF/AICR index. The three indices investigated in this thesis could be a practical way to examine how different populations adhere to overall and specific recommendations for prevention of cancer and chronic diseases, and to measure dietary and lifestyle patterns.

List of abbreviations

AICR	American Institute for Cancer Research
BMI	Body mass index
BP	Blood pressure
CRC	Colorectal cancer
CRC-NORDIET	The Norwegian dietary guidelines and colorectal cancer survival study
CVD	Cardiovascular disease
DALY	Disability-adjusted life-year
DASH	Dietary Approaches to Stop Hypertension
DBP	Diastolic blood pressure
FFQ	Food frequency questionnaire
HbA1c	Hemoglobin A1c
HDL-c	High-density lipoprotein cholesterol
HEI	Healthy Eating Index
LDL-c	Low-density lipoprotein cholesterol
NCD	Non-communicable disease
NFBDG	Norwegian food-based dietary guidelines
RCT	Randomized controlled trial
SBP	Systolic blood pressure
SD	Standard deviation
TAG	Triglycerides
TC	Total cholesterol
UPF	Ultra-processed food
VISA	The Vascular lifestyle-intervention and screening in pharmacies study
WCRF	World Cancer Research Fund
WHO	World Health Organization

List of figures

Figure 1: Flow diagram of included and excluded participants in the current thesis
Figure 2: Adherence to the NFBDG diet index in the CRC-NORDIET population
Figure 3: Adherence to the components in the NFBDG diet index in the CRC-NORDIET
population
Figure 4: Adherence to the NFBDG lifestyle index in the CRC-NORDIET population27
Figure 5: Adherence to the components in the NFBDG lifestyle index in the CRC-NORDIET
population
Figure 6: Adherence to the WCRF/AICR index in the CRC-NORDIET population28
Figure 7: Adherence to the components in the WCRF/AICR index in the CRC-NORDIET
population
Figure 8: Adherence to the NFBDG diet index in the VISA population
Figure 9: Adherence to the components in the NFBDG diet index in the VISA population 30
Figure 10: Adherence to the NFBDG lifestyle index in the VISA population
Figure 11: Adherence to the components in the NFBDG lifestyle index in the VISA
population
Figure 12: Adherence to the WCRF/AICR index in the VISA population
Figure 13: Adherence to the components in the WCRF/AICR index in the VISA population

List of tables

Table 1: The NFBDG diet index and the NFBDG lifestyle index
Table 2: The WCRF/AICR index
Table 3: Demographic and clinical characteristics of the participants of the CRC-NORDIET
study and the VISA study, in total and stratified by gender
Table 4: Mean adherence score to the NFBDG diet index, the NFBDG lifestyle index and the
WCRF/AICR index in the CRC-NORDIET study, in total and stratified by gender25
Table 5: Mean adherence score to the NFBDG diet index, the NFBDG lifestyle index and the
WCRF/AICR index in the VISA study, in total and stratified by gender
Table 6: Adherence to the NFBDG indices and the WCRF/AICR index and associations to
blood pressure, plasma lipids and BMI in the CRC-NORDIET population
Table 7: Adherence to the NFBDG indices and the WCRF/AICR index and associations to
blood pressure, plasma lipids and BMI in the VISA population

Table of contents

Acknowledgements	III
Abstract	V
List of abbreviations	VI
List of figures	VII
List of tables	VIII
1 Background	1
1.1 Non-communicable diseases	1
1.1.1 Colorectal cancer	2
1.1.2 Role of diet and lifestyle in CRC	2
1.1.3 Cardiovascular disease	3
1.1.4 Role of diet and lifestyle in CVD	4
1.2 Dietary patterns and dietary- and healthy indices	5
1.2.1 Dietary- and healthy indices and health outcomes	6
1.2.2 The WCRF/AICR index	7
1.2.3 The Norwegian food-based dietary guidelines indices	8
1.2.4 Dietary assessment methods	10
1.2.5 The role of indices in CRC and CVD	11
2 Objectives	12
3 Methods	13
3.1 The CRC-NORDIET study	13
3.1.1 Study design	13
3.1.2 Study population	13
3.1.3 Assessment methods	14
3.2 The VISA study	14
3.2.1 Study design and subjects	14
3.2.2 Assessment methods	15
3.3 The master's thesis	15
3.3.1 Study design and subjects	15
3.3.2 Data collection and processing	15
3.3.3 Operationalization of the NFBDG diet index and the NFBDG lifestyle index	16
3.3.4 Operationalization of the WCRF/AICR index	18
3.3.5 Statistical analyses	20
3.3.6 Ethics	20
3.3.7 Contributions	20

4 Results	21
4.1 Subject characteristics	21
4.1.1 Intake of food groups and drinks	22
4.2 Adherence to the NFBDG indices and the WCRF/AICR index in the CRC-NORDI population	
4.2.1 Adherence to the NFBDG diet index	
4.2.2 Adherence to the components in the NFBDG diet index	
4.2.3 Adherence to the NFBDG lifestyle index	
4.2.4 Adherence to the components in the NFBDG lifestyle index	
4.2.5 Adherence to the WCRF/AICR index	
4.2.6 Adherence to the components in the WCRF/AICR index	
4.3 Adherence to the NFBDG indices and the WCRF/AICR index in the VISA populat	tion
4.3.1 Adherence to the NFBDG diet index	
4.3.2 Adherence to the components in the NFBDG diet index	
4.3.3 Adherence to the NFBDG lifestyle index	
4.3.4 Adherence to the components in the NFBDG lifestyle index	
4.3.5 Adherence to the WCRF/AICR index	
4.3.6 Adherence to the components in the WCRF/AICR index	
4.4 Adherence to the NFBDG indices and the WCRF/AICR index and associations to clinical factors in both populations	
4.4.1 Associations between the indices and clinical factors in the CRC-NORDIET population	33
4.4.2 Associations between the indices and clinical factors in the VISA population	33
5 Discussion	36
5.1 Methodological considerations	36
5.1.1 Assessment of dietary intake and adherence to the indices	36
5.1.2 Operationalization of the NFBDG indices and the WCRF/AICR index	38
5.1.3 The role of dietary indices in nutritional research	39
5.2 Discussion of results	40
5.2.1 Study populations	40
5.2.2 Adherence to the NFBDG indices in the CRC-NORDIET population	41
5.2.3 Adherence to the WCRF/AICR index in the CRC-NORDIET population	42
5.2.4 Adherence to the NFBDG indices in the VISA population	44
5.2.5 Adherence to the WCRF/AICR index in the VISA population	45
5.2.6 Gender differences in adherence to the indices	46
5.2.7 Associations between adherence to the indices and clinical factors	
5.3 Strengths and limitations	48

6 Conclusions	
7 Future perspectives	50
References	
Supplementary files 1-6	59

1 Background

1.1 Non-communicable diseases

In 2019, seven of the top ten leading causes of death in the world were non-communicable diseases (NCDs), also known as chronic diseases (1, 2). The term NCD includes cardiovascular diseases (CVDs), cancers, chronic respiratory diseases, diabetes, and a number of other chronic diseases (1). According to the World Health Organization (WHO), NCDs accounted for 74 % of all deaths globally in 2019, and death from these diseases are on the rise (1). Furthermore, NCDs contribute to a substantial part of disability-adjusted life-years (DALYs) in the world, which is a measure of the overall disease burden (i.e. expressed as years lost due to disability from disease or early death) (3). In Norway, nine of the top ten causes of DALYs in 2019 were NCDs, and cancer and CVD are currently the main causes of death (4, 5).

The NCDs have in common that they are complex multifactorial diseases, as they are a result of several risk factors combined, such as genetics, environment, and behavior (2). Behavioral risk factors include unhealthy diet, tobacco use, excessive alcohol use and physical inactivity (2). In a global perspective, the prevalence of smoking has decreased, but it is still an important risk factor of NCDs, and tobacco use is contributing to about 15 % of DALYs in the adult population (6, 7). For alcohol, low to moderate intakes have been associated with decreased risk of CVD and mortality from CVD. However, higher intakes of alcohol increase the risk of cancer and CVD, as well as increase the risk of death from these diseases, thereby diminishing the possible preventive effects at low intakes (8). In addition to smoking and alcohol, physical inactivity and unhealthy diets are important risk factors of chronic diseases and death from these (6, 9, 10). In 2017, unhealthy diets contributed to 11 million deaths and 255 million DALYs among adults, through increasing the prevalence of chronic diseases such as CVD and cancers (10).

According to the WHO and the World Cancer Research Fund (WCRF), most CVD cases and 30-50 % of the most common cancers, including colorectal cancer (CRC) might be preventable through a more healthy behavior and lifestyle, in terms of smoking cessation,

physical activity, reduced alcohol intake and having a healthy diet (11-14). This represents a challenge, but also yields a great potential in the prevention of these diseases.

1.1.1 Colorectal cancer

The term CRC includes cancer of the colon and the rectum (13). Worldwide, CRC is the second and third most commonly occurring type of cancer in women and men, respectively (13), accounting for more than 1.9 million new cases in 2020 for both genders (15). CRC causes more than 900 000 deaths annually, and by this qualifies to be the second most common cause of death from cancer (15, 16). There are large geographical differences in the incidence of CRC, with the highest incidences seen in Western countries (13, 16). According to the Cancer Registry of Norway, 4295 new cases were registered in Norway in 2019 (17). The incidence trend of colon cancer in Norwegian women has increased over the past decade, whereas the rate has levelled off for men. The incidence of rectal cancer has remained stable since the 1990s in both genders (17). The five-year relative survival rate has steadily improved since 1965 to about 70 % in 2019 for both colon and rectal cancer in both genders. The high incidence of CRC and the improvement in the survival rates result in a growing population of CRC survivors (17).

1.1.2 Role of diet and lifestyle in CRC

There are several established risk factors of CRC (13). However, most CRC cases do not have one clear cause, but rather seem to be a result of several factors in combination. Age, hereditary conditions and inflammatory bowel disease are examples of non-modifiable risk factors (13, 18), while factors related to diet and lifestyle such as dietary pattern, physical activity and smoking are examples of modifiable risk factors of CRC (13). An overall healthy dietary pattern may reduce the risk of cancer more than one dietary factor in isolation (11).

In 1997 and 2007, the WCRF and the American Institute for Cancer Research (AICR) published the first and second Expert Reports, respectively. These publications summarized the existing scientific literature on food, nutrition and physical activity in relation to cancer prevention and survival in a global perspective (19). The second report included ten lifestyle recommendations for cancer prevention (20), aiming to reduce the risk of cancer through a healthy diet, physical activity and having a healthy body weight (11). Nevertheless, a lot of research has been conducted in the cancer field, and in 2018 the third Expert Report from the

WCRF/AICR was published (20). The recommendations from this report are similar to those from 2007, however, they emphasize a more holistic approach to diet and lifestyle and promote healthy dietary- and lifestyle patterns (20). In the report, evidence on the separate dietary and lifestyle factors in relation to the risk of CRC are classified as limited or strong (13). The report states that there is strong evidence that smoking, excessive alcohol consumption, high consumption of red and processed meat and obesity increases the risk of CRC, and that physical activity, intake of whole grains, foods containing dietary fiber, dairy products and calcium supplements decreases the risk (13). It is also suggested a protective effect of the intake of foods containing vitamin C, fish, vitamin D and multivitamin supplements, but the evidence is limited (13).

Currently, there are no official specific diet and lifestyle recommendations after a cancer diagnosis, other than to follow the recommendations for primary cancer prevention (13). However, several studies have investigated the effect of diet and lifestyle in CRC survivors (21-25). A systematic review and meta-analysis of prospective observational studies, suggested that high versus low levels of physical activity after a CRC diagnosis significantly reduce total mortality (relative risk (RR)=0.58, 95 % CI: 0.48-0.70) and CRC-specific mortality (RR=0.61, 95 % CI: 0.40-0.92) (22). In addition, a risk reduction in mortality was also suggested among CRC survivors with increased level of physical activity from pre- to post-diagnosis compared to those who did not change their level of physical activity or were inactive before diagnosis (22, 26). Concerning diet, it has been proposed that a high intake of refined carbohydrates, red and processed meat and sugar-sweetened beverages after diagnosis may increase the risk of recurrence of disease and mortality (25). However, the data is limited, and more randomized intervention studies are needed (23, 25).

The prevalence of comorbidities among CRC patients are common (27). About 40 % have at least one comorbid condition established, and studies have shown an increased risk of overall mortality among these patients (27, 28). The most commonly occurring comorbidities in CRC patients include chronic respiratory disease, diabetes and CVD (27, 29).

1.1.3 Cardiovascular disease

CVDs can be defined as disorders of the heart and blood vessels, as for instance hypertension, coronary heart disease, stroke, heart failure and other conditions related to the heart and vessels (14). CVD is often caused by atherosclerosis, an inflammatory process in which

arteries are occluded due to accumulation of lipids and inflammatory cells in the arterial walls (30, 31). According to the WHO, CVDs are the leading cause of death in the world, accounting for almost 18 million deaths annually (1, 14). According to the Norwegian Institute of Public Health, 21 % of the entire Norwegian population have established CVD or high risk of developing the disease. Approximately 1.1 million inhabitants are medically treated, either for prevention or as treatment of established disease (32). Nevertheless, this number is predicted to increase in the future, due to several reasons, such as decreased prevalence of smoking, improved treatment and higher survival rates from CVD (32). In addition, a larger proportion of the CVD cases are of less severity, thus patients live longer after the onset of disease (32, 33).

1.1.4 Role of diet and lifestyle in CVD

Risk factors of CVD include lifestyle factors such as tobacco use, excessive alcohol intake, inadequate physical activity and unhealthy diet (34, 35), as well as physiological factors like increased age, male gender, high blood pressure, elevated hemoglobin A1c, and dyslipidemia (i.e. elevated low-density lipoprotein cholesterol (LDL-c), total cholesterol (TC) and triglycerides (TAG), and lowered high-density lipoprotein cholesterol (HDL-c)) (14, 36). As mentioned above, CVD is commonly occurring among CRC patients, and is also a comorbidity of other chronic diseases such as type 2 diabetes mellitus, rheumatoid arthritis and osteoarthritis, chronic obstructive pulmonary disease and other cancers. Thus, having one or more of these conditions increases the risk of CVD (27, 37, 38).

Both high blood pressure and dyslipidemia, which are major risk factors of CVD, have been studied in relation to dietary and lifestyle factors (30, 31, 39). A diet low in sodium, high in fruits and vegetables and alcohol in moderation (i.e. one and two drinks per day for women and men, respectively), as well as weight loss, have been found to reduce blood pressure in both hypertensive and non-hypertensive individuals (30). The mentioned dietary factors, in addition to increased intake of low-fat dairy, whole grains, poultry, fish and nuts, together with a decreased intake of fats, red meat, sweets and sugar-sweetened beverages, are what characterizes the Dietary Approaches to Stop Hypertension (DASH) dietary pattern (40). This dietary pattern is well studied, and a diet in accordance with this is often recommended in treatment of hypertension (39, 40). Intake of fiber, fat, proteins and vitamin C in association to blood pressure have been studied, but the effects are uncertain (30). The main dietary focus

in studies concerning dyslipidemia, has been on the intake of fat and the fat quality. A reduced risk of cardiovascular events through improvements in plasma lipid profile has been reported in a number of studies (34, 41-43). The risk reduction has been found among participants that replace their intake of saturated fatty acids (e.g. meat and meat products, high-fat dairy) with intake of monounsaturated and polyunsaturated fatty acids (e.g. vegetable oils, nuts, fatty fish) (30, 34).

1.2 Dietary patterns and dietary- and healthy indices

The diet can be seen as a multidimensional exposure, as we consume a variety of combinations of foods, food groups, drinks and nutrients. Foods and nutrients alone or in combination act synergistically, and a change in one part of the diet is often accompanied by another compensatory change (44, 45). An overall healthy diet (e.g. in accordance with the WCRF/AICR recommendations or DASH dietary pattern) may be more beneficial rather than focusing on the intake of single foods or nutrients. Studies of individual nutrients and food items have provided important information on the relationship between diet and health outcomes such as CRC and CVD, but these studies do not consider the whole diet. Thus, the focus in nutritional epidemiology has gradually changed towards focusing on the diet in total and dietary patterns (46).

In order to assess a dietary pattern, *dietary indices* can be used. However, some indices include information on lifestyle factors (i.e. physical activity, smoking, body weight) in addition to the dietary components, and are thereby referred to as *healthy indices*. Several dietary and healthy indices have been developed (47-51). The different types of indices can be categorized into groups on the basis of their origin (47, 52); 1) general recommendations from an authority (i.e. the Healthy Eating Index-2015 (HEI-2015), the WCRF/AICR index), 2) culture and tradition (i.e. the healthy Nordic food index, the Mediterranean diet score), 3) a posteriori derived from the diet of the study population (derived empirically by principal component analysis or factor analysis) or 4) generated from existing scientific literature (i.e. the Dietary Inflammatory Index) (47, 52). Common for the indices based on general recommendations, culture and tradition or existing literature, is the a priori determination of dietary patterns (53).

1.2.1 Dietary- and healthy indices and health outcomes

Adherence to an index indicates how well the participant complies with each component as well as the total score of the index. Despite the differences in how the indices are developed and what their basis are, a general approach is that a higher score reflects a higher and better adherence to the index. Several studies have investigated the association between adherence to any index and health outcomes (11, 48-52). However, multiple methods for determining and evaluating dietary and lifestyle patterns exist, which makes the comparability of findings across studies challenging (54). Regardless of the variations and diversity between indices and challenges in how to compare findings, dietary and healthy indices seem to capture the essential components of a healthy diet and lifestyle. The directions of associations seem to be consistent when it comes to different health outcomes (52, 55).

Several outcomes can be investigated by using dietary and healthy indices. Changes in dietary pattern in a population over time (56), how well a population adhere to specific recommendations (57), association to mental health outcomes (58), association to biomarkers of inflammation or hemostasis (59, 60), association to type 2 diabetes mellitus (61) or prediction of health outcomes (62) are some examples of what indices can be used for. However, the most commonly used approach is to investigate the association between an index and risk of NCD such as CVD and cancer, or mortality (48, 62, 63).

Reedy and coworkers (62) investigated the relationship between adherence to four indices (HEI-2015, the alternative HEI-2010, the alternate Mediterranean Diet and DASH) and allcause, CVD and cancer mortality in an American population of older adults. Almost 500 000 participants were included in the study with a follow-up of 15 years. They found that higher scores of adherence were associated with a 12-28 % lower risk of death from all-cause, CVD and cancer for all of the included indices (62). These findings were supported by Hu *et al.* (48) in a cohort of 12 400 middle-aged Americans. They investigated the four same indices as Reedy *et al.* (62). When comparing participants in the highest and lowest quintiles of adherence score to the HEI-2015, Hu *et al.* observed a 32 % lower risk of CVD mortality and an 18 % lower risk of all-cause mortality in the participants in the highest quintiles. A 16 % lower risk of incident CVD was also found. Similar risk reductions were found for the other indices included in the study (48). Consistent with the reported findings for overall mortality risk, Olsen *et al.* (63) found that a 1-point increment in a healthy Nordic food index was associated with a significantly lower risk of death in a Danish cohort of men and women (63). Concerning CVD and risk factors of CVD, studies show some disagreement. A recently published Finnish study by Tertsunen *et al.*, did not find it evident that higher adherence to a healthy Nordic food index was associated with lower risk of coronary heart disease nor CVD risk factors such as blood pressure (BP) and plasma lipids (64). When investigating BP and association to the DASH, Nordic diet and Mediterranean diet indices in a systematic review and meta-analysis by Ndanuko *et al.*, a significant inverse association was found between adherence to each separate index and systolic and diastolic BP (65). Similar results were found in a population of type 2 diabetes patients (66). Low values of plasma lipids, BP, hemoglobin A1c (HbA1c) and body mass index (BMI) were associated with a higher adherence to the Mediterranean diet score (66).

The risk of cancer or cancer-specific mortality in association to index adherence has been investigated by several studies (11, 51, 52, 62, 67, 68). Kyrø et al. (51) investigated the association between adherence to the healthy Nordic food index and incidence of CRC. They found that women with the highest adherence, had a 35 % lower risk of CRC compared to those of lowest adherence. The findings in men showed a similar trend of lower risk the higher adherence, but the results were not significant (51). An inverse association between CRC and adherence to the WCRF/AICR index has also been reported by Solans and coworkers in a systematic review and meta-analysis (11). Their findings suggested a 14 % risk reduction in CRC per point increment in the index score (RR=0.86, 95 % CI: 0.82-0.89). In addition, they found inverse associations between each 1-point increment in index adherence and risk of breast cancer (RR=0.90. 95 % CI: 0.87-0.93), lung cancer (RR=0.93, 95 % CI: 0.89-0.96), overall mortality (RR=0.90, 95 % CI: 0.84-0.96) and cancer-specific mortality (RR=0.91, 95 % CI: 0.89-0.92) (11). Similar findings for cancer mortality were reported by Steck et al. and Reedy et al. when investigating the relationship with adherence to the HEI-2010, the alternative HEI-2010, the alternate Mediterranean diet and DASH indices (52, 62).

1.2.2 The WCRF/AICR index

As already mentioned, indices have been constructed in order to measure adherence to the recommendations from the WCRF/AICR expert reports (11, 69). The indices are developed on the same basis, but there are some variations in which recommendations that are included and cut-off points used. Thus, there are some limitations in the direct comparability of the

results from these studies (11, 70). In order to measure adherence to the most recent WCRF/AICR recommendations (20), and to more easily be able to compare the findings across populations and countries, a standardized scoring system (the WCRF/AICR 2018 index, hereafter referred to as the *WCRF/AICR index*) was developed by Shams-White and coworkers (70). Of the ten recommendations published in the third report, eight were included in the index (i.e. healthy weight, physical activity, whole grains/fruits/vegetables/beans, ultra-processed foods (UPFs), red/processed meat, sugar-sweetened beverages, alcohol, and for mothers; breastfeeding). The recommendation on dietary supplement use and recommendations for cancer survivors were not included. Each of the mentioned components is scored as 0 for low adherence, 0.5 for moderate adherence or 1 for high adherence. The total score is thus ranging from 0-7 (8 if breastfeeding is included). As for most indices, a higher score reflects a better adherence to the recommendations (70).

The associated risk of cancer and different cancer types with adherence to the WCRF/AICR index have been investigated in several studies (68, 71-75). The risk of total cancer was investigated in two Swedish prospective cohort studies of men and women, and a 12 % reduced risk of total cancer was found when comparing those of highest adherence scores to those of lowest (72). The risk of breast cancer, CRC, prostate cancer and pancreatic cancer has also been investigated, all reporting significant inverse associations for participants of highest adherence compared to lowest adherence (RR=0.73 and OR=0.60 for breast cancer (68), HR=0.79 for CRC (75), OR=0.81 for prostate cancer (73) and HR=0.67 for pancreatic cancer (74)).

1.2.3 The Norwegian food-based dietary guidelines indices

In Norway, the tradition of providing dietary guidelines from the health authorities to the population dates back to the 1950s (76). Since then, the guidelines have been updated several times, with the most recent update published in 2011. During the decades, recommendations on physical activity have been included in addition to the dietary recommendations. Today, the Norwegian food-based dietary guidelines (NFBDG) include 13 recommendations on both dietary and lifestyle factors, aiming to prevent chronic diet- and lifestyle-related diseases such as cancer and CVD (76).

To estimate the adherence to the dietary intervention in the Norwegian dietary guidelines and colorectal cancer survival (CRC-NORDIET) study (described in section 3.1), two new indices

based on the NFBDG have recently been developed by researchers in the CRC-NORDIET study at the Department of Nutrition, University of Oslo (Hege Berg Henriksen, personal communication, January 2021) (77, 78), namely the *NFBDG diet index* and the *NFBDG lifestyle index*.

The NFBDG diet index

The NFBDG diet index consists of twelve dietary components: 1) fruits and berries, 2) vegetables, 3) whole grains, 4) unsalted nuts, 5) fish, 6) low-fat dairy, 7) margarine/oils, 8) red meat, 9) processed meat, 10) foods high in sugar and fat, 11) sugar-sweetened beverages, and 12) dietary supplements. Each of these components are weighed equally. Similarly to the WCRF/AICR index (70), the adherence to each component is scored three-leveled; as 0 (low adherence), 0.5 (moderate adherence) or 1 (high adherence), which makes it possible to score a total of 12 points. The three-leveled approach also makes it possible to distinguish individuals whose lifestyle habits approach, but does not fulfill the recommendations, from those whose lifestyle habits more clearly deviate from the recommendations. Hence, the potential benefit from moderate adherence to a recommendation is taken into account (67, 70). The exact cut-off values for each of the dietary components are described in detail in the validation study of the NORDIET-FFQ used in the CRC-NORDIET study (77) and also in section 3.3.3.

The NFBDG lifestyle index

The NFBDG lifestyle index includes five components: 1) diet, 2) body fatness, 3) physical activity, 4) tobacco use and 5) alcohol. As in the NFBDG diet index, each of these components are equally weighed and scored three-leveled (0, 0.5 and 1 points), meaning total score in the NFBDG lifestyle index ranges from 0-5 points. The dietary component is based on the NFBDG diet index, in which a total score of 0-4 points is defined as low adherence (0 points), 4.5-8 points is defined as moderate adherence (0.5 points) and more than 8 points is defined as total adherence (1 point) in the NFBDG lifestyle index. The body fatness score is based on body mass index, and physical activity is based on the total time spent on physical activity in moderate- to- vigorous intensity per week. Tobacco use is based on whether or not the participant use to smoke. Alcohol is based on the participants' intake in grams per day.

In the current NFBDG, the recommendations on fruits and berries, vegetables, whole grains, fish, red meat, margarine/oils, alcohol and physical activity are quantitatively defined (76). The recommendations on unsalted nuts, low-fat dairy, foods high in sugar and fat, processed

meat and sugar-sweetened beverages are qualitative, with no quantified limit for recommended intake (76). In the validation study of the NORDIET-FFQ, the qualitative recommendations were translated into quantitative limits (77). Thus, these are used in the NFBDG indices, as well as the already quantified limits. The recommendations on BMI and smoking were not included in the NFBDG, but were included to the NFBDG lifestyle index due to their known associations to health outcomes (7, 79). The cut-off points for the included components in the two NFBDG indices are based on exciting literature (67, 70) and have been discussed. The development of these two indices makes it possible to assess the dietary and lifestyle patterns of the participants of the CRC-NORDIET study with regards to the NFBDG, and to estimate how well they adhere to the dietary intervention in the study. Nevertheless, this also yields the potential to investigate how well different populations or groups adhere to the NFBDG.

1.2.4 Dietary assessment methods

When studying the relationship of diet or dietary patterns on disease and health outcomes, there is a need of methods to measure the intake of foods, nutrients and beverages on individual or group level (80, 81). Several methods can be used, each providing slightly different information on the participant's diet. Some methods estimate the average intake over a longer time period (i.e. food frequency questionnaire (FFQ)), whereas others provide information of the consumption in detail (i.e. weighed records, 24-hour recall (24-HR)) in a more recent time-period (80). Whichever method used, the true intakes cannot be measured with absolute certainty, and the methods are prone to measurement errors it is important to be aware of when interpreting effects of dietary intake on health outcomes (81).

Food frequency questionnaire

Generally, the dietary assessment methods can be categorized as retrospective or prospective, according to whether the past or current food intake is recorded (81). The most widely used method for assessing dietary intake is the FFQ, a retrospective method that can estimate usual intake over a specific period of time (i.e. weeks, months, years) (80, 81). The FFQ consists of two main components – a food list and a frequency response section, and some FFQs include questions on portion sizes as well. The number of food items included in the food list varies between the different FFQs, and the information obtained can thereby vary in level of detail. The method has several advantages, including having the ability to assess the usual intake

over a given time period and to range the individual intakes, assess intakes on a group level, being easy to complete, can be self-administered by the participants, and the processing is often done inexpensively by computers. The error of day-to-day consumption is minimized, and the method does not affect eating behavior. The method is an appropriate method to be used in large studies if self-administered (80, 82, 83).

The dietary information used to investigate dietary patterns and categorize participants' adherence to a dietary index, can be obtained from different dietary assessment methods. However, since FFQ is the most used method for collecting dietary data, this is likely to be the most used method to measure adherence to an index (11, 52).

1.2.5 The role of indices in CRC and CVD

While the WCRF/AICR index is established, the NFBDG diet index and the NFBDG lifestyle index are still under development and need to be tested and implemented. To the best of our knowledge, no studies have investigated the adherence to the WCRF/AICR index in any Norwegian population. Adherence to the new NFBDG indices have not yet been investigated. Thus, information on how a population of CRC patients and a population of healthy individuals with moderately elevated risk of CVD adhere to these three indices, could provide valuable information on the dietary and lifestyle patterns related to prevention of chronic diseases and cancer in these populations.

2 Objectives

The present master's thesis was conducted as a subproject of the CRC-NORDIET study (78) and the Vascular lifestyle-intervention and screening in pharmacies (VISA) study (84). Because of the joint role of diet and lifestyle in the development and risk of both CRC and CVD (12, 14), we wanted to examine the adherence to dietary and healthy indices in the participants included in these two studies. The overall objective of this thesis was therefore to investigate adherence to the new NFBDG indices and the established WCRF/AICR index in two distinct study populations at baseline in both studies. More specifically:

Primary aim:

• Investigate the adherence to the NFBDG diet index, the NFBDG lifestyle index and the WCRF/AICR index in CRC patients (the CRC-NORDIET population) and healthy individuals with an elevated risk of CVD (the VISA population) at baseline.

Secondary aims:

- Investigate the adherence to the specific components of the three indices in the CRC-NORDIET population and the VISA population at baseline.
- Study gender differences in adherence to the three indices in the two populations at baseline.
- Investigate the association between adherence to the indices and plasma lipids (i.e. total cholesterol, triglycerides), blood pressure, and body mass index at baseline.

3 Methods

3.1 The CRC-NORDIET study

3.1.1 Study design

The CRC-NORDIET study is a multicenter, two-armed, randomized controlled trial (RCT) that has its study center situated at the Department of Nutrition, University of Oslo, Norway. Most previous studies have investigated lifestyle factors and the risk of CRC in the general population, and few have focused on the effect of a healthy lifestyle on disease-free- and overall survival post-diagnosis of CRC. This was the background for initiation of the study (78). The enrollment of participants (n=500) started in March 2012 and finished during December 2020. The overall objective of the study is to investigate how a diet in accordance with the NFBDG affects long-term disease outcomes and survival after a CRC diagnosis, and a number of secondary outcomes will also be examined (78). Eligible patients were recruited from Oslo University Hospital and Akershus University Hospital within the South-Eastern Norway Regional Health Authority and were invited to the baseline of the study. The patients accepting the invitation were randomly allocated to either intervention (n=250) or control group (n=250) prior to baseline. The participants had to sign a written informed consent before the randomization was performed (78).

3.1.2 Study population

The study population are men and women aged 50-80 years old, newly diagnosed with nonmetastatic CRC (International classification of diseases (ICD)-10 18-20) and Tumor Node Metastasis (TNM) stage I-III. Participants were not eligible if they had metastases, were unable to read and understand Norwegian, had conditions making it difficult to understand or perceive the intervention (i.e. dementia, altered mental status, total parenteral nutrition) or if participating in other RCTs in conflict with the CRC-NORDIET trial (78). All participants of the study are followed up at the study center on several occasions (enrollment of study (baseline), 6 months, 12 months and 3, 5, 7, 10 and 15 years after baseline of study) (78).

3.1.3 Assessment methods

At baseline, the participants in both study groups are asked to complete several questionnaires, which include information on their dietary intake and physical activity. A validated short food frequency questionnaire (NORDIET-FFQ) (77) is used to assess the dietary habits of the participants. Other measurements and biological sampling include anthropometry (i.e. height, body weight, BMI, waist and hip circumference), BP and blood lipids (i.e. TC, TAG). Information on smoking was available from activity sensors and from another dietary questionnaire completed at baseline (78).

NORDIET-FFQ

The NORDIET-FFQ (**Supplementary file 1**) is a 65-item semi-quantitative FFQ developed and validated by Henriksen *et al.* (77) in the CRC-NORDIET study. The questionnaire is designed to estimate adherence to the NFBDG and to measure compliance to the dietary intervention in the study. It covers dietary intake (grams per day) and physical activity (minutes per day) for the previous 1-2 months. Sixty-three food items cover the intake of fruits, berries, nuts, vegetables, cereals, beverages, cakes, sweet candy, breads and spreads, oils, margarine and butter, dairy products, fish, meat, rice, pasta and dietary supplements. The questionnaire includes two questions on physical activity with moderate and vigorous intensity (77, 78).

3.2 The VISA study

3.2.1 Study design and subjects

The VISA study is a multicenter RCT performed in 50 community pharmacies in Norway with a parallel three-arm design, conducted in 2014-2015 (84). It was initiated and aimed to investigate the effect of alerting and/or giving simple dietary and lifestyle advice for CVD risk reduction compared to a control group that did not receive alert nor advice. The study was performed in a healthy population (e.g. no previous CVD or CVD-related medications) with moderately elevated risk of CVD, in terms of slightly elevated risk factors that rarely give symptoms such as BP, plasma lipids and HbA1c. Of the about 1300 voluntary individuals screened for participation, 582 participants met the inclusion criteria (i.e. moderately elevated risk of CVD) and were thus included in the VISA study. All participants had to sign a written informed consent (84).

3.2.2 Assessment methods

Information on background, smoking, physical activity and dietary habits of the participants were self-reported through a background questionnaire and a FFQ (85). Biochemical and anthropometric measurements were performed by pharmacy staff, and included measuring of plasma lipids (TC, HDL-c, LDL-c and TAG), HbA1c, BP, height and weight (84).

VISA-FFQ

The VISA-FFQ (**Supplementary file 2**) was used to assess dietary intake at baseline and every follow-up. It is a 62-item semi-quantitative FFQ adapted from the NORDIET-FFQ (77), but with a greater emphasize on food items associated with CVD (85). The transformation of food items contributing to intakes of different fatty acids from the NORDIET-FFQ to the VISA-FFQ was performed in order to collect broader information on foods containing a high amount of saturated fatty acids and other foods known to affect total cholesterol levels. The transformation included alteration of 14 items, adding 4 items and removal of 9 items (85). Forty-four items remained the same in the VISA-FFQ as in the NORDIET-FFQ. Further information on the transformation is described elsewhere (85). All questionnaires were optical scanned and transformed into data files, and handled as the NORDIET-FFQs as described in further detail in Henriksen *et al.* 2018 (77, 85).

3.3 The master's thesis

3.3.1 Study design and subjects

This current master's thesis was a cross-sectional designed subproject of the CRC-NORDIET study and the VISA study, using data from the two studies collected at baseline of each study. It was initiated in August 2020 and finished in May 2021. Criteria for participant inclusion to this thesis comprised age 50-80 years and completion of the study specific dietary questionnaire (i.e. NORDIET-FFQ, VISA-FFQ) at baseline.

3.3.2 Data collection and processing

Dietary intake and physical activity were assessed using the NORDIET-FFQ and the VISA-FFQ completed at baseline, which formed the basis of measuring adherence to the indices (i.e. the NFBDG diet index, the NFBDG lifestyle index and the WCRF/AICR index). Information on smoking was collected from the activity sensors or a long FFQ in the CRC-NORDIET study, and from the VISA-FFQ in the VISA study. Anthropometric measurements (i.e. weight, height, BMI), demographics (i.e. gender, age, level of education, marital status), BP and plasma lipid measurements (i.e. TC, TAG) were available from the databases of each study. For the participants in the CRC-NORDIET study, information on tumor localization and TNM-stage were retrieved from electronic patient records.

The NORDIET-FFQs were scanned by the master student and others, and the image files were transformed into data files using Cardiff Teleform 2006 Software (6.0) (Datascan). The main supervisor (Hege Berg Henriksen) of the current master's thesis is a super-user of Cardiff Teleform and was responsible for teaching and following up the master student in using this method. The questionnaires were checked for completeness by the researchers. Missing values were handled by the following rules: 1) if frequency was reported, but amount missing, the lowest amount was registered; 2) if amount was reported, but frequency missing, the lowest frequency above 0 was registered; 3) if both frequency and amount were missing, they remained as missing values; 4) if frequency was registered as 0, but amount was reported, the registered amount was removed; 5) if two frequencies or amounts were reported, a mean value was calculated and reported. The scanning and handling of the VISA-FFQs were completed by researchers in the VISA study group and followed a similar protocol as for the NORDIET-FFQ (77).

3.3.3 Operationalization of the NFBDG diet index and the NFBDG lifestyle index

The NFBDG diet index, the NFBDG lifestyle index and how they were operationalized in the current thesis is shown in **Table 1**. A three-leveled scoring system was used (0, 0.5 and 1) for all components except for the use of dietary supplements and tobacco, where a binary score was used (0 and 1). Low, moderate and high adherence was indicated by 0, 0.5 and 1 points, respectively. The score of each component was summarized to construct the final score, hence a total score of 12 points in the NFBDG diet index and 5 points in the NFBDG lifestyle index. The questions in the FFQs contributing to each component in the score, was as described previously in the validation of the NORDIET-FFQ (77). Intake of dietary supplements was not included in the VISA-FFQ (85), hence the recommendation on dietary supplement use was not operationalized in the VISA study.

NFBDG diet index		Recommendation/ cut-	Points				
NFI	bDG alet maex	Recommendation/ cut-	0	0.5	1		
1	Fruits and berries	≥250 g/d		<125 g/d	125-<250 g/d	≥250 g/d	
2	Vegetables	≥250 g/d	<125 g/d	125-<250 g/d	≥250 g/d		
3	Whole grains	Women: ≥70 g/d Men: ≥90 g/d	Women: Men:	<35 g/d <45 g/d	35-<70 g/d 45-<90 g/d	≥70 g/d ≥90 g/d	
4	Unsalted nuts	BMI<25: ≥20 g/d BMI≥25: 20-<30 g/d	<10 g/d <10 g/d, ≥30 g/d	10-<20 g/d 10-<20 g/d	≥20 g/d 20-<30 g/d		
5	Fish	≥43 g/d	<21.5 g/d	21.5-<43 g/d	≥43 g/d		
6	Low-fat dairy	≥100 g/d	<50 g/d	50-<100 g/d	≥100 g/d		
7	Margarine/oils	margarine or soft margar	Users of cooking oil, liquid margarine or soft margarine and non-users of butter with high content of saturated fatty acids			Healthy margarine/ oils	
8	Red meat	≤71 g/d		≥71 g/d	35.5-<71 g/d	<35.5 g/d	
9	Processed meat	≤20 g/d		>20 g/d	10-20 g/d	<10 g/d	
10	Foods high in sugar and fat	≤20 g/d		>20 g/d	10-20 g/d	<10 g/d	
11	Sugar-sweetened drinks	≤20 g/d	>20 g/d	10-20 g/d	<10 g/d		
12	Dietary supplements ^a	0 units/d		>0	-	0	
	Total score					12	

Table 1: The NFBDG diet index and the NFBDG lifestyle index

NFBDG lifestyle index

1	Diet	See dietary components included. Maximum score 12 points.	0-4	5-8	9-12
2	Body weight	Normal weight, measured in BMI (kg/m ²)	<18.5 or ≥30	25-29.9	18.5-24.9
3	Physical activity	Moderate/vigorous physical activity 150 min/week	<75	75-<150	≥150
4	Tobacco	0	>0	-	0
5	Alcohol	0 g/d	>30 g/week (4.29 g/d) ethanol	30 g/week (4.29 g/d) ethanol	0
	Total score				5

^aNot operationalized in the VISA study. Abbreviations: BMI; body mass index, NFBDG; Norwegian food-based dietary guidelines.

3.3.4 Operationalization of the WCRF/AICR index

The operationalization of the WCRF/AICR recommendations in the current thesis was done as by Shams-White and coworkers (70) when the required information for the component was available. **Table 2** provides an overview of how the recommendations were operationalized in the paper by Shams-White *et al.* (70) and in this thesis. The recommendation on breastfeeding was not relevant for the current thesis and was therefore not included in the total score.

The score of the individual components was summarized to construct the total adherence score, which had a range from minimal 0 to maximum 7 points. For each recommendation, a three-leveled score was used. Zero, 0.5 and 1 points were given for low, moderate or high adherence to the recommendation, respectively. The cut-off values for each component are described in Table 2. Each component contributed equally to the total score. If the component included sub-recommendations, each of the sub-recommendations were scored as 0 (low adherence), 0.25 (moderate adherence) and 0.5 (high adherence) points, and then summarized to create the total component score. Seven points indicated total adherence to the recommendations. In this thesis, the recommendations on physical activity, red and processed meat, sugar-sweetened beverages and alcohol were operationalized as described by Shams-White et al. (70). Otherwise, we did not have information on all participants regarding waist circumference, hence only BMI was used. With respect to the third component in the index, we scored the participants using the intake of whole grains, fruits and vegetables. Beans were included in the original index, but the FFQs used in this thesis did not provide information on intake of beans. Information on fiber intake was not available, thus it was not included. For the fourth component (i.e. UPFs), we used intake of foods high in starch, fats and sugars to score the participants, rather than calculating percentage of total kcals from UPFs, which was the original approach. This was performed because the FFQs used in the thesis did not provide enough information on the foods included in the NOVA classification system of UPFs (86), and they are not designed to estimate total energy intake (77).

Table 2: The WCRF/AICR index

	CRF/AICR commendation	Operationalization of recommendation in Shams- White <i>et al.</i> (70)	Operationalization in the master's thesis	Points			
1	Be a healthy weight	BMI (kg/m ²): 18.5-24.9 25-29.9 <18.5 or ≥30 Waist circumference (cm): Men: <94 Women: <80 Men: 94-<102 Women: 80-<88 Men: ≥102 Women: ≥88	- BMI (kg/m ²): 18.5-24.9 25-29.9 <18.5 or ≥30	1 0.5 0			
2	Be physically active	Total moderate-vigorous physical activity (min/week): ≥150 75-<150 <75	Total moderate-vigorous physical activity (min/week): ≥ 150 1 $75-<150$ 0.5 <75 0				
3	Eat a diet rich in whole grains, vegetables, fruits and beans	Fruits and vegetables (g/day): \geq 400 200-400 <200 Total fiber (g/day): \geq 30 15-<30 <15	Fruits and vegetables (g/day) : ≥ 400 200-400 <200 Total whole grain (g/day) : ≥ 70 35-<70 <35	$\begin{array}{c} 0.5\\ 0.25\\ 0\\ 0.5\\ 0.25\\ 0\\ 0.25\\ 0\\ \end{array}$			
4	Limit consumption of «fast foods» and other processed foods high in fat, starches or sugars	Percent of total kcals from ultra- processed foods (aUPFs): Tertile 1 Tertile 2 Tertile 3	Total foods high in sugar and fat (g/day): <10 10-20 >20	1 0.5 0			
5	Limit consumption of red and processed meat	Total red meat (g/week) and processed meat (g/week): Red meat <500 and processed meat <21 Red meat <500 and processed meat 21-<100 Red meat >500 or processed meat ≥100	Total red meat (g/day) and processed meat (g/day): Red meat <35.5 and processed meat <3 Red meat 35.5-71 and processed meat 3-14.3 Red meat >71 or processed meat >14.3	1 0.5 0			
6	Limit consumption of sugar-sweetened drinks	Total sugar-sweetened drinks (g/day): 0 >0-<250 >250	Total sugar-sweetened drinks (g/day): 0 >0-≤250 >250	1 0.5 0			
7	Limit alcohol consumption	Total ethanol (g/day): 0 >0-<28 (2 drinks) males and ≤ 14 (1 drink) females >28 (2 drinks) males and >14 (1 drink) females	Total ethanol (g/day): 0 >0-<28 (2 drinks) males and ≤ 14 (1 drink) females >28 (2 drinks) males and >14 (1 drink) females	1 0.5 0			
8	For mothers: breastfeed your baby, if you can (optional)	Exclusively breastfeed over lifetime for a total of: 6+ months >0-<6 months Never erican Institute for Cancer Research	Not included				

Abbreviations: AICR; American Institute for Cancer Research, aUPFs; adapted ultra-processed foods, BMI; body mass index, WCRF; World Cancer Research Fund.

3.3.5 Statistical analyses

All variables were checked for normal distribution by evaluating histograms, normal Q-Q plots and Kolmogorov-Smirnov tests (p>0.05). Demographic and clinical characteristics are presented as mean with standard deviation (SD)/median with percentiles (25th and 75th percentiles) for normally/non-normally distributed continuous variables and as count with percent for categorical variables. Independent samples t-tests/Mann-Whitney U tests were used in comparative analyses between genders within each study population, as well as between the two study populations in demographic and clinical characteristics. Adherence to the three indices is presented in tables as mean (SD) and in figures as percentages of participants within each category of adherence. One-way between-groups analysis of variance (ANOVA)/Kruskal-Wallis tests were used in comparison of groups of low, moderate and high adherence to each index. P<0.05 was considered statistically significant. IBM SPSS Statistics version 27 was used for all statistical analyses.

3.3.6 Ethics

The CRC-NORDIET study is approved by the Regional Committees for Medical and Health Research Ethics (REC Protocol Approval 2011/836, **Supplementary file 3**) and by the data protection officials in Oslo University Hospital and Akershus University Hospital. Biological samples and materials are stored in a biobank at University of Oslo. The study was registered on the National Institutes of Health Clinical Trials (<u>www.ClinicalTrials.gov</u>; Identifier: NCT01570010) (78). The VISA study was approved by the Norwegian Regional Ethical Committee Health South-East (REC number 2013/1660, **Supplementary file 4**), and was registered on the National Institutes of Health Clinical Trials, identifier NCT 02223793 (84).

3.3.7 Contributions

The student retrieved and handled dietary data from the NORDIET-FFQs, and performed the statistical analyses linked to the aims of the thesis in close collaboration with the supervisors. As a member of the research team conducting the CRC-NORDIET study, the student contributed to several tasks, including dietary counselling at the study center and by telephone and data collection from the participants during the measuring days at the study center (i.e. BP and anthropometric measurements). Previously collected data in the CRC-NORDIET study and the VISA study were also available for this thesis.

4 Results

In total, 503 participants were included in the CRC-NORDIET study and 582 participants in the VISA study. Of these, 494 participants of the CRC-NORDIET study and 381 participants of the VISA study were included in the current thesis, as shown in **Figure 1**.

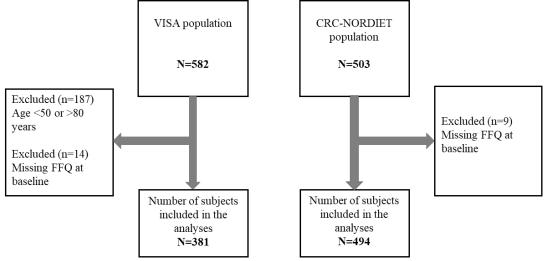


Figure 1: Flow diagram of included and excluded participants in the current thesis. In order to have age balance, 187 participants in the VISA population were excluded, and 14 participants were excluded due to missing FFQ at baseline. Nine participants of the CRC-NORDIET study were excluded due to missing FFQ at baseline.

Abbreviations: CRC-NORDIET; the Norwegian dietary guidelines and colorectal cancer survival study, FFQ; food frequency questionnaire, VISA; the Vascular lifestyle-intervention and screening in pharmacies study.

4.1 Subject characteristics

Demographic and clinical characteristics of the included participants in the two studies (CRC-NORDIET and VISA) are presented in **Table 3**, stratified by gender. The gender distribution was 54 % men and 46 % women in the CRC-NORDIET study and 25 % men and 75 % women in the VISA population.

In the CRC-NORDIET population, the mean age was 66 years and median BMI was 26.4 kg/m². Most participants were classified as normal weight (35 %) or overweight (45 %) (87), were married/cohabitant (71 %), highly educated (49 %) and were non-smokers (90 %) (**Table 3**). Compared to women, men had significantly higher BMI (p<0.001) and different marital status (p<0.001). Colon cancer (C18) was the most frequent tumor location (59 %) followed by cancer of the rectum (C20, 36 %). Mean number of days since surgery was 162 and 88 % had completed treatment at the baseline visit. Twenty-six percent of the participants had a stoma (**Supplementary file 5**).

In the VISA population, the mean age was 63 years and median BMI was 26.0 kg/m². As in the CRC-NORDIET population, most participants had a normal weight (40 %) or overweight (40 %) and were married/cohabitant (61 %). Forty-one percent were educated from college/university, and 42 % had high school as their highest completed education. Eighty-three percent did not smoke. Men had significantly lower age (p=0.02), higher BMI (p=0.02) and different marital status (p=0.01) than women (**Table 3**).

Concerning risk factors of CVD (BP, HbA1c, TC, TAG, LDL- and HDL-cholesterol) of the included participants, median BP in the CRC-NORDIET population was 124/72 mmHg, median TAG 1.3 mmol/l and median TC 5.4 mmol/l, as shown in **Table 3**. In the CRC-NORDIET population, women had significantly lower systolic blood pressure (SBP) and diastolic blood pressure (DBP) and higher TC compared to men (p<0.001 for all). In the VISA population, median BP was 136/82 mmHg, median TAG 1.8 mmol/l and TC 6.8 mmol/l. Compared to men, women had significantly lower SBP (p=0.008) and DBP (p=0.02), and higher TC and HDL-c (p<0.001 for both).

4.1.1 Intake of food groups and drinks

The estimated intake of the main food groups and drinks included in the NFBDG indices and the WCRF/AICR index are shown in **Supplementary file 6**. There were several significant differences between men and women within the two studies. In the CRC-NORDIET population, women had significantly higher intake of fruits and berries (p=0.001) and vegetables (p<0.001) and significantly lower intake of low-fat dairy (p=0.05), red meat (p<0.001), processed meat (p<0.001), sugar-sweetened beverages (p=0.002) and alcohol (p<0.001) than men. The VISA population showed some similarities; women had significantly higher intake of vegetables (p=0.001) and significantly lower intake of red meat (p=0.009), processed meat (p<0.001), sugar-sweetened beverages (p<0.001) and alcohol (p<0.001) than men. Also, men in the VISA population had significantly higher intake of foods high in sugar and fat than women (p=0.02).

In the next two sections, adherence to different indices will be presented separately for the CRC-NORDIET study (chapter 4.2) and the VISA study (chapter 4.3).

Table 3: Demographic and clinical characteristics of the participants of the CRC-NORDIET study and the VISA study, in total and stratified by gender

	CRC-NORDIET (n=494)				VISA (n=381	p-values ^a			
	Total	Men	Women	Total	Men	Women	p_1	p ₂	p ₃
Age (years), mean ± SD	65.6 ± 7.7	65.9 ± 7.7	65.2 ± 7.6	63.4 ± 7.6	61.8 ± 7.4	63.9 ± 7.6	<0.001	0.30	0.02
Weight (kg), mean ± SD	79.9 ± 16.2	87.1 ± 13.9	71.6 ± 14.7	75.1 ± 13.7	85.0 ± 12.3	71.9 ± 12.5	<0.001	<0.001	<0.001
Height (cm), mean ± SD	172.7 ± 8.7	178.3 ± 6.4	166.1 ± 6.0	167.8 ± 7.5	176.5 ± 5.1	165.0 ± 5.8	<0.001	<0.001	<0.001
DMI $(l_{1}\sigma/m^2)^{b}$ modion (D D) ^c	26.4 (23.5,	26.9 (24.7,	25.4 (22.3,	26.0 (23.8,	26.8 (24.8,	25.6 (23.6,	0.76	<0.001	0.03
BMI $(kg/m^2)^b$, median $(P_{25}, P_{75})^c$	29.3)	29.5)	28.7)	29.1)	29.7)	28.9)	0.70	<0.001	0.02
BMI categories (kg/m ²), n (%)							0.26	<0.001	0.01
Underweight <18.5	6 (1.2)	0 (0)	6 (2.6)	2 (0.5)	0 (0)	2 (0.7)			
Normal weight 18.5-24.9	171 (34.6)	73 (27.5)	98 (42.8)	153 (40.2)	26 (27.7)	127 (44.3)			
Overweight 25-29.9	220 (44.5)	139 (52.5)	81 (35.4)	152 (39.9)	50 (53.2)	102 (35.5)			
Obese ≥30	97 (19.6)	53 (20.0)	44 (19.2)	74 (19.4)	18 (19.1)	56 (19.5)			
Gender, n (%)							<0.001		
Men	265 (53.6)			94 (24.7)					
Women	229 (46.4)			287 (75.3)					
Marital status, n (%)							<0.001	<0.001	0.01
Married/cohabitant	344 (71.2)	206 (79.5)	138 (61.6)	229 (60.9)	69 (74.2)	160 (56.5)			
Previously married	95 (19.7)	33 (12.7)	62 (27.7)	118 (31.4)	20 (21.5)	98 (34.6)			
Single	44 (9.1)	20 (7.7)	24 (10.7)	29 (7.7)	4 (4.3)	25 (8.8)			
Highest completed education, n							0.007	0.00	0.10
(%)							0.005	0.86	0.10
Primary school	46 (9.5)	26 (9.9)	20 (9.0)	61 (16.9)	16 (17.8)	45 (16.6)			
High school	200 (41.3)	109 (41.6)	91 (41.0)	152 (42.1)	31 (34.4)	121 (44.6)			
College/university (1-3 years)	122 (25.2)	68 (26.0)	54 (24.3)	84 (23.3)	29 (32.2)	55 (20.3)			
College/university (>4 years)	116 (24.0)	59 (22.5)	57 (25.7)	64 (17.7)	14 (15.6)	50 (18.5)			
Smoking status, n (%)							0.006	1.0	0.99
Smoker	49 (10.1)	26 (10.0)	23 (10.2)	63 (16.7)	15 (16.1)	48 (16.9)			
Non-smoker	437 (89.9)	234 (90.0)	203 (89.8)	314 (83.3)	78 (83.9)	236 (83.1)			

(Table 3 continued)

Blood pressure (mmHg), median	L								
(P25, P75) ^c									
Systolic	124.3 (113.0, 137.0)	127.5 (116.0, 139.0)	122.0 (109.5, 132.3)	136.0 (122.5, 147.8)	140.5 (125.8, 152.5)	134.0 (122.0, 145.5)	<0.001	<0.001	0.008
Diastolic	71.5 (64.5, 78.0)	74.5 (69.3, 81.0)	67.5 (62.0, 74.5)	82.0 (75.0, 89.3)	84.5 (78.5, 91.0)	82.0 (74.5, 88.5)	<0.001	<0.001	0.02
Triglycerides (mmol/l), median (P25, P75) ^c	1.3 (1.1, 1.8)	1.3 (1.1, 1.9)	1.3 (1.1, 1.8)	1.8 (1.3, 2.6)	1.9 (1.3, 2.8)	1.8 (1.2, 2.5)	<0.001	0.75	0.38
Total cholesterol (mmol/l), median (P ₂₅ , P ₇₅) ^c	5.4 (4.7, 6.1)	5.1 (4.4, 5.8)	5.8 (5.0, 6.4)	6.8 (6.2, 7.4)	6.5 (5.6, 7.2)	6.9 (6.3, 7.5)	<0.001	<0.001	<0.001
LDL-cholesterol (mmol/l), median (P ₂₅ , P ₇₅) [°]	NA	NA	NA	4.1 (3.6, 4.8)	4.0 (3.3, 4.6)	4.2 (3.6, 4.7)			0.13
HDL-cholesterol (mmol/l), median (P ₂₅ , P ₇₅) ^c	NA	NA	NA	1.7 (1.4, 2.1)	1.4 (1.1, 1.7)	1.8 (1.5, 2.2)			<0.001
HbA1c (%), median (P25, P75) ^c	NA	NA	NA	5.6 (5.4, 5.8)	5.6 (5.4, 5.9)	5.6 (5.4, 5.8)			0.70

^aIndependent samples t-test or Mann-Whitney U test for continuous variables and chi-square tests for categorical variables, p-values for the differences between CRC-NORDIET and VISA populations in total (p_1) , men and women of the CRC-NORDIET study (p_2) and men and women of the VISA study (p_3) . P<0.05 was considered statistically significant (marked in bold).

^bCalculated as weight in kilograms divided by height in meters squared (kg/m²).

^cP₂₅=25th percentile, P₇₅=75th percentile.

Abbreviations: BMI; body mass index, CRC-NORDIET; the Norwegian dietary guidelines and colorectal cancer study, HbA1c; hemoglobin A1c, HDL; high-density lipoprotein, LDL; low-density lipoprotein, NA; not available, SD; standard deviation, VISA; the Vascular lifestyle-intervention and screening in pharmacies study.

4.2 Adherence to the NFBDG indices and the

WCRF/AICR index in the CRC-NORDIET population

Adherence to the NFBDG diet index, NFBDG lifestyle index, and WCRF/AICR index in the CRC-NORDIET population is described in the following sections. The mean adherences varied from 45 % in the NFBDG diet index, to 52 % in the WCRF/AICR index and 57 % in the NFBDG lifestyle index (Table 4). The mean adherence scores were 5.4 (±SD 1.6) of 12 points in the NFBDG diet index, 2.9 (±SD 0.8) of 5 points in the NFBDG lifestyle index, and 3.6 (±SD 1.0) of 7 points in the WCRF/AICR index. Mean adherence scores were significantly higher in women than in men (p<0.001 for the NFBDG diet index and the WCRF/AICR index, p=0.001 for the NFBDG lifestyle index).

Table 4: Mean adherence score to the NFBDG diet index, the NFBDG lifestyle index and the WCRF/AICR index in the CRC-NORDIET study, in total and stratified by gender

Inder	Tota	ıl	Men		Won	b	
Index	Mean \pm SD	% ₀a	Mean \pm SD	% a	$Mean \pm SD$	Mean \pm SD % ^a	
NFBDG diet index ^c	5.4 ± 1.6	44.8	5.1 ± 1.5	42.3	5.7 ± 1.7	47.6	<0.001
NFBDG lifestyle index ^d	2.9 ± 0.8	57.0	2.7 ± 0.8	54.8	3.0 ± 0.9	59.6	0.001
WCRF/AICR index ^e	3.6 ± 1.0	51.7	3.4 ± 0.9	48.9	3.8 ± 1.0	54.9	<0.001

^aPercentage of maximum score.

^bIndependent samples t-test, p-value for the differences in adherence score between men and women.

^cScore ranging from 0-12 points. ^dScore ranging from 0-5 points.

^eScore ranging from 0-7 points.

Abbreviations: AICR; American Institute for Cancer Research, NFBDG; the Norwegian food-based dietary guidelines, SD; standard deviation, WCRF; World cancer research fund.

Women Men Women Men Women Women Men Women Men Women Men Women Men Men

2*

3*

1*

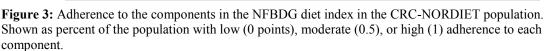
100 % 90 % 80 % 70 % 60 % 50 %

40 %

30 % 20 % 10 % 0 %

1

0.5 **0**



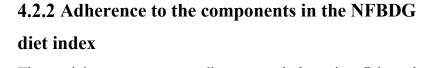
5

4

1; fruits and berries, 2; vegetables, 3; whole grains, 4; unsalted nuts, 5; fish, 6; low-fat dairy, 7; margarine/oils, 8; red meat, 9; processed meat, 10; foods high in sugar and fat, 11; sugar-sweetened beverages, 12; dietary supplements.

6*

*p<0.05, chi-square test for the differences between men and women.



4.2.1 Adherence to the NFBDG diet index

higher in women as compared to men (p=0.001).

Most participants (72 %) were moderate adherent to the

NFBDG diet index, and only a small percentage (4 %) had

high adherence (Figure 2). The adherence was significantly

The participants were most adherent to whole grains, fish, and sugar-sweetened beverages, and least adherent to unsalted

nuts, processed meat, foods high in sugar and fat and dietary supplements (Figure 3). For the recommendations on fruits and berries, vegetables and red meat, most participants had moderate to high adherence. More women than men fulfilled the recommendations on fruits and berries, vegetables, whole grains, red meat, processed meat and sugar-sweetened beverages, whereas more men than women fulfilled the recommendation on low-fat dairy products (p<0.05).

adherence.

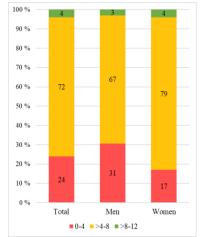


Figure 2: Adherence to the NFBDG diet index in the CRC-NORDIET population. The red color indicates low adherence, yellow moderate, and green high

Men Women

10

Men

7

Women

8*

Men Women

0*

Women

11*

Men

Men Women

12

4.2.3 Adherence to the NFBDG lifestyle index

Most participants (42 %) were moderate adherent to the NFBDG lifestyle index, with a score of >2 to 3 points, whereas few very fully (>4 points) or very low (<1 points) adherent (**Figure 4**). More women were moderate to high adherent (34 %) as compared to men (25 %), which was also found to be significantly different (p=0.004)

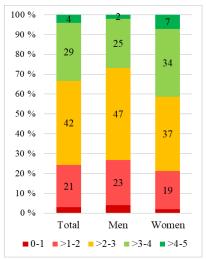


Figure 4: Adherence to the NFBDG lifestyle index in the CRC-NORDIET population.

4.2.4 Adherence to the components in the NFBDG lifestyle index

Physical activity and tobacco use were the components most participants were adherent to in both genders (**Figure 5**). Very few fulfilled the recommendation on alcoholic intake, and for diet, most participants were categorized within the range of moderate score of adherence. More women fulfilled the recommendation on alcoholic intake and had a healthy weight (i.e. BMI) as compared to men (p<0.05).

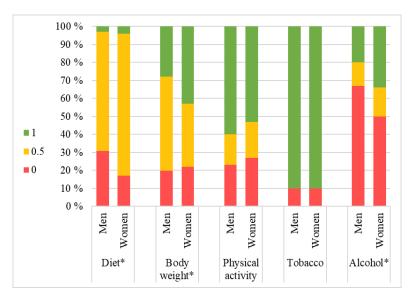


Figure 5: Adherence to the components in the NFBDG lifestyle index in the CRC-NORDIET population. Shown as percent of the population with low (0 points), moderate (0.5), or high (1) adherence to each component.

*p<0.05, chi-square test for the differences between men and women.

4.2.5 Adherence to the WCRF/AICR index

In adherence to the WCRF/AICR index, most of the total population (37 %) and most men (42 %) were moderate adherent (>3 to 4 points) (**Figure 6**). Most women were moderate adherent (30 %) or in the categories above. No participants were in the category of lowest adherence (0-1 points), and very few were in the category of highest adherence (>6 points). Women showed significantly higher adherence compared to men (p<0.001).



Figure 6: Adherence to the WCRF/AICR index in the CRC-NORDIET population.

4.2.6 Adherence to the components in the WCRF/AICR index

As illustrated in **Figure 7**, both genders showed best adherence to the components of healthy weight, physical activity and sugar-sweetened beverages, and poorest adherence to the components of foods high in sugar and fat, and red and processed meat. Most participants were moderate adherent to the recommendations on fruits, vegetables and whole grains and alcohol. Compared to men, more women were adherent to the recommendations on fruits, vegetables and whole grains, red and processed meat, sugar-sweetened beverages and alcohol, and had a healthy weight (i.e. BMI) (p<0.05).

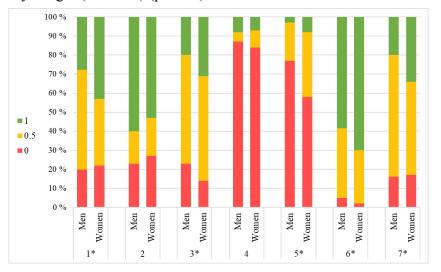


Figure 7: Adherence to the components in the WCRF/AICR index in the CRC-NORDIET population. Shown as percent of the population with low (0 points), moderate (0.5), or high (1) adherence to each component.

1; healthy weight, 2; physical activity, 3; fruits, vegetables and whole grains, 4; foods high in sugar and fat, 5; red and processed meat, 6; sugar-sweetened beverages, 7; alcohol.

*p<0.05, chi-square test for the differences between men and women.

4.3 Adherence to the NFBDG indices and the WCRF/AICR index in the VISA population

Adherence to the three indices in the VISA population is described below. Overall, the mean adherence was 46 % in the NFBDG diet index, 53 % in the WCRF/AICR index and 61 % in the NFBDG lifestyle index (**Table 5**). The mean adherence scores were 5.1 (\pm SD 1.5) of 11 points in the NFBDG diet index, 3.1 (\pm SD 0.8) of 5 points in the NFBDG lifestyle index, and 3.7 (\pm SD 0.9) of 7 points in the WCRF/AICR index. Women had significantly higher adherence to the NFBDG diet index and the WCRF/AICR index than men (p<0.001 for both), whereas no significant difference was observed in adherence to the NFBDG lifestyle index.

Table 5: Mean adherence score to the NFBDG diet index, the NFBDG lifestyle index and the WCRF/AICR index in the VISA study, in total and stratified by gender

Index	Total		Men	I I	Won	p b	
	Mean \pm SD	% ⁰a	Mean \pm SD	% a	$Mean \pm SD$	‰ ^a	- r
NFBDG diet index ^c	5.1 ± 1.5	46.2	4.5 ± 1.5	40.7	5.3 ± 1.4	47.9	<0.001
NFBDG lifestyle index ^d	3.1 ± 0.8	61.4	2.9 ± 0.8	58.8	3.1 ± 0.8	62.4	0.051
WCRF/AICR index ^e	3.7 ± 0.9	53.0	3.4 ± 0.9	47.9	3.8 ± 0.9	54.6	<0.001

^aPercentage of maximum score.

^bIndependent samples t-test, p-value for the differences in adherence score between men and women.

^cScore ranging from 0-11 points (the component regarding dietary supplements was not included).

^dScore ranging from 0-5 points.

^eScore ranging from 0-7 points.

Abbreviations: AICR; American Institute for Cancer Research, NFBDG; Norwegian food-based dietary guidelines, SD; standard deviation, WCRF; World cancer research fund.

4.3.1 Adherence to the NFBDG diet index

As shown in **Figure 8**, 70 % of the participants were moderate adherent the NFBDG diet index, whereas 29 % had low adherence. More women than men were moderate adherent, and the difference was significant (p=0.046).

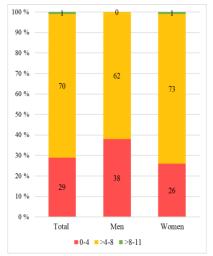


Figure 8: Adherence to the NFBDG diet index in the VISA population. The red color indicates low adherence, yellow moderate, and green high adherence.

4.3.2 Adherence to the components in the NFBDG diet index

Both genders were most adherent to the recommendations on whole grains, fish, low-fat dairy, margarine/oils and sugar-sweetened beverages (**Figure 9**). Most participants did not fulfill the recommendations on unsalted nuts, red meat, processed meat and foods high in sugar and fat. Compared to men, more women adhered to the recommendations on vegetables, whole grains and sugar-sweetened beverages (p<0.05).

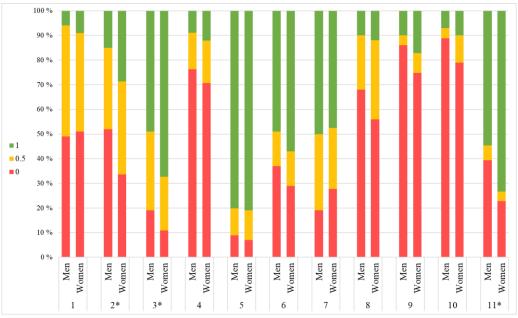


Figure 9: Adherence to the components in the NFBDG diet index in the VISA population. Shown as percent of the population with low (0 points), moderate (0.5), or high (1) adherence to each component.

1; fruits and berries, 2; vegetables, 3; whole grains, 4; unsalted nuts, 5; fish, 6; low-fat dairy, 7; margarine/oils, 8; red meat, 9; processed meat, 10; foods high in sugar and fat, 11; sugar-sweetened beverages. *p<0.05, chi-square test for the differences between men and women.

4.3.3 Adherence to the NFBDG lifestyle index

Most participants were moderate adherent (40 %) or showed moderate to high adherence (41 %) to the NFBDG lifestyle index, as illustrated in **Figure 10**. Very few were in the lowest and highest adherence categories. No significant difference was observed between the genders.



Figure 10: Adherence to the NFBDG lifestyle index in the VISA population.

4.3.4 Adherence to the components in the NFBDG lifestyle index

Both genders were most adherent to the recommendation on tobacco, followed by physical activity (**Figure 11**). Very few had an intake of alcoholic drinks classified as low adherence, and very few were fully adherent to the dietary component. More women than men had a healthy body weight (i.e. BMI), and were adherent to the dietary component (p<0.05).

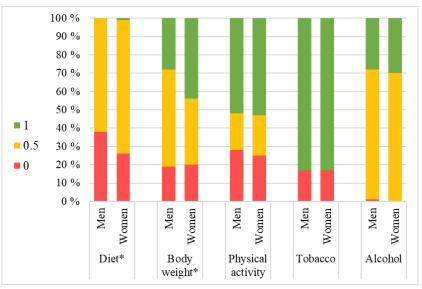


Figure 11: Adherence to the components in the NFBDG lifestyle index in the VISA population. Shown as percent of the population with low (0 points), moderate (0.5), or high (1) adherence to each component.

*p<0.05, chi-square test for the differences between men and women.

4.3.5 Adherence to the WCRF/AICR index

The majority of both men (44 %) and women (39 %) were moderate adherent to the WCRF/AICR index (**Figure 12**). More women (33 %) than men (12 %) were in the category above moderate, whereas more men (33 %) than women (19 %) were in the category below. Very few were in the lowest (0-1 points) and highest (>6-7 points) adherence categories. Women showed significantly higher adherence than men (p=0.001).

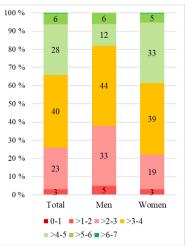


Figure 12: Adherence to the WCRF/AICR index in the VISA population.

4.3.6 Adherence to the components in the WCRF/AICR index

Most participants fulfilled the recommendations on sugar-sweetened beverages and physical activity (**Figure 13**). Foods high in sugar and fat and red and processed meat were the components were most participants did not fulfil the recommendations. Almost all participants fulfilled the recommendation of low or none alcoholic intake. More women fulfilled the recommendations on healthy weight, fruits, vegetables and whole grains, and sugar-sweetened beverages, as compared to men (p<0.05).

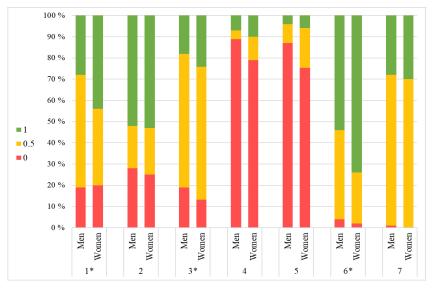


Figure 13: Adherence to the components in the WCRF/AICR index in the VISA population. Shown as percent of the population with low (0 points), moderate (0.5), or high (1) adherence to each component.

1; healthy weight, 2; physical activity, 3; fruits, vegetables and whole grains, 4; foods high in sugar and fat, 5; red and processed meat, 6; sugar-sweetened beverages, 7; alcohol.

*p<0.05, chi-square test for the differences between men and women.

4.4 Adherence to the NFBDG indices and the WCRF/AICR index and associations to clinical factors in both populations

The final aim was to investigate the associations between the three indices and clinical factors such as BP, plasma lipids (TAG and TC) and BMI in the two separate populations (the CRC-NORDIET population and the VISA population). In order to do so, adherence to each index was grouped into low, moderate and high (i.e. red, yellow and green colors).

4.4.1 Associations between the indices and clinical factors in the CRC-NORDIET population

Table 6 shows the associations between adherence to any of the indices and clinical factors in the CRC-NORDIET population. For the NFBDG diet index, a significant difference across the adherence groups was observed in TAG (p=0.03), but no significant differences were observed in pairwise comparisons. Across the groups of adherence to the NFBDG lifestyle index, a significant inverse association was observed in TAG and BMI (p<0.001). For the WCRF/AICR index, a similar inverse association between adherence and BMI was observed (p<0.001). Compared to the group with low adherence, those with high adherence to the WCRF/AICR index had lower TAG (p<0.001) and higher TC (p=0.048).

4.4.2 Associations between the indices and clinical factors in the VISA population

Associations between adherence to any of the indices and clinical factors in the VISA population are shown in **Table 7**. Compared to those of low adherence to the NFBDG diet index, those of moderate adherence had significantly higher TC (p=0.02). For the NFBDG lifestyle index, a significant inverse association between adherence and DBP and BMI was observed across all groups of adherence (p<0.001). Additionally, the participants of high adherence to the NFBDG lifestyle index had significantly lower TAG as compared to low adherence (p=0.04). Across the groups of adherence to the WCRF/AICR index, a significant inverse association in BMI was observed (p<0.001). There was also a significantly lower DBP (p<0.001) and higher TC (p=0.006) in the participants of high adherence as compared to the participants of low adherence.

	Tatal	NFBDG diet index					NFBDG lif	estyle index		WCRF/AICR index			
	Total	0-4	>4-8	>8-12	p ^a	0-2	>2-3	>3-5	p ^a	0-3	>3-4	>4-7	p ^a
Participants, n	494	119	355	17		117	204	162		156	181	157	
Female, n (%)	229	38 (31.9)	180	10 (58.8)	0.001	48 (41.0)	84 (41.2)	93 (57.4)	0.003	65 (41.7)	69 (38.1)	95 (60.5)	<0.001
	(46.4)		(50.7)										
Age (years),	$65.6 \pm$	$64.8 \pm$	$66.0 \pm$	$62.7 \pm$	0.09	$65.4 \pm$	$65.6 \pm$	$65.8 \pm$	0.90	$65.1 \pm$	$65.8 \pm$	$65.7 \pm$	0.70
mean ± SD	7.7	8.3	7.4	8.2		7.7	7.6	7.7		8.0	7.5	7.5	
SBP (mmHg),	124.3	123.5	124.5	125.5	0.73	125.0	125.5	123.5	0.29	124.0	126.0	123.0	0.11
median (P25,	(113.0,	(115.0,	(113.0,	(104.0,		(115.5,	(114.5,	(111.4,		(113.1,	(117.0,	(108.8,	
P 75) ^b	137.0)	134.5)	138.0)	135.0)		137.8)	138.0)	135.1)		137.0)	138.0)	136.5)	
DBP (mmHg),	71.5	70.5	72.0	73.0	0.86	71.0	72.0	71.8	0.30	71.0	73.0	71.5	0.052
median (P25,	(64.5,	(66.0,	(64.0,	(65.0,		(64.5,	(65.5,	(63.5,		(64.5,	(66.5,	(63.3,	
P 75) ^b	78.0)	78.5)	78.0)	82.8)		78.0)	79.0)	77.0)		76.9)	80.5)	77.0)	
TAG (mmol/l),	1.3 (1.1,	1.5 (1.1,	1.27	1.2 (1.0,	0.03	1.6 (1.1,	1.4 (1.0,	1.2 (1.0,	<0.001	1.5 (1.2,	1.4 (1.1,	1.1 (1.0,	<0.001
median (P25,	1.8)	2.1)	(1.01,	1.4)		2.0)	2.0)	1.5)		2.0)	1.9)	1.6)	
P 75) ^b			1.76)										
TC (mmol/l),	5.4 (4.7,	5.3 (4.7,	5.45	5.04	0.60	5.5 (4.7,	5.3 (4.6,	5.6 (4.7,	0.28	5.2 (4.5,	5.3 (4.5,	5.7 (5.0,	0.009
median (P25,	6.1)	5.9)	(4.64,	(4.4, 5.9)		6.2)	5.9)	6.1)		5.9)	5.9)	6.3)	
P 75) ^b			6.10)										
BMI $(kg/m^2)^c$,	26.4	26.9	26.3	25.1	0.08	28.8	26.8	23.9	<0.001	28.3	26.5	24.0	<0.001
median (P25,	(23.5,	(24.3,	(23.3,	(21.0,		(26.3,	(24.8,	(22.0,		(26.0,	(23.8,	(22.2,	
P 75) ^b	29.3)	29.3)	29.3)	27.2)		31.7)	29.4)	26.4)		31.3)	28.6)	26.8)	

Table 6: Adherence to the NFBDG indices and the WCRF/AICR index and associations to blood pressure, plasma lipids and BMI in the CRC-NORDIET population

^aChi-square test for categorical variables and one-way ANOVA or Kruskal-Wallis test for continuous variables, p-value for the differences between the different groups of adherence within each index.

^bP₂₅=25th percentile, P₇₅=75th percentile.

°Calculated as weight in kilograms divided by height in meters squared (kg/m²).

Abbreviations: AICR; American Institute for Cancer Research, BMI; body mass index, DBP; diastolic blood pressure, NFBDG; the Norwegian food-based dietary guidelines, SBP; systolic blood pressure, TAG; triglycerides, TC; total cholesterol, WCRF; World cancer research fund.

	Tatal	NFBDG diet index				NFBDG lifestyle index				WCRF/AICR index			
	Total	0-4	>4-8	>8-11	p ^a	0-2	>2-3	>3-5	p ^a	0-3	>3-4	>4-7	p ^a
Participants, n	381	110	268	3		58	151	172		99	153	129	
Female, n (%)	287	74 (67.3)	210	3 (100.0)	0.046	39 (67.2)	115	133	0.29	63 (63.6)	112	112	<0.001
	(75.3)		(78.4)				(76.2)	(77.3)			(73.2)	(86.8)	
Age (years),	$63.4 \pm$	$63.1 \pm$	$63.5 \pm$	$64.7 \pm$	0.82	$61.0 \pm$	$62.9 \pm$	$64.7 \pm$	0.003	$62.1 \pm$	$63.6 \pm$	$64.2 \pm$	0.10
mean ± SD	7.6	8.1	7.4	5.1		7.4	7.6	7.4		7.7	8.1	6.6	
SBP (mmHg),	136.0	137.0	135.0	121.5	0.25	142.0	135.0	134.3	0.18	139.0	135.0	134.5	0.08
median (P25,	(122.5,	(123.5,	(122.5,	(113.5,		(125.4,	(124.0,	(120.35,		(127.0,	(121.0,	(121.5,	
P 75) ^b	147.8)	149.6)	146.9)	129.5)		150.6)	146.5)	146.9)		152.0)	145.5)	146.3)	
DBP (mmHg),	82.0	83.5	81.5	80.0	0.39	86.5	83.5	79.5	<0.001	86.0	80.5	80.5	<0.001
median (P25,	(75.0,	(77.1,	(75.0,	(70.3,		(81.6,	(76.0,	(73.5,		(80.5,	(73.5,	(74.5,	
P 75) ^b	89.3)	90.1)	88.9)	86.0)		92.5)	90.0)	87.5)		92.0)	87.0)	88.5)	
TAG (mmol/l),	1.8 (1.3,	1.8 (1.2,	1.8 (1.3,	2.3 (1.7,	0.93	1.9 (1.4,	1.9 (1.3,	1.6 (1.2,	0.02	1.8 (1.4,	1.8 (1.3,	1.8 (1.2,	0.46
median (P25,	2.6)	2.5)	2.6)	2.7)		3.0)	2.6)	2.5)		2.7)	2.6)	2.5)	
P 75) ^b													
TC (mmol/l),	6.8 (6.2,	6.5 (6.1,	6.9 (6.3,	5.9 (5.8,	0.02	6.6 (6.0,	6.8 (6.1,	6.9 (6.3,	0.20	6.4 (6.0,	6.9 (6.2,	6.9 (6.3,	0.005
median (P25,	7.4)	7.2)	7.5)	7.0)		7.5)	7.4)	7.5)		7.2)	7.4)	7.6)	
P 75) ^b													
BMI $(kg/m^2)^c$,	26.0	26.1	25.9	29.2	0.63	29.5	27.2	24.6	<0.001	28.2	26.5	24.3	<0.001
median (P25,	(23.8,	(24.2,	(23.6,	(25.3,		(25.0,	(24.6,	(22.8,		(25.4,	(24.2,	(22.3,	
P 75) ^b	29.1)	29.4)	29.0)	32.2)		31.7)	30.7)	26.8)		31.3)	29.1)	26.3)	

Table 7: Adherence to the NFBDG indices and the WCRF/AICR index and associations to blood pressure, plasma lipids and BMI in the VISA population

^aChi-square test for categorical variables and one-way ANOVA or Kruskal-Wallis test for continuous variables, p-value for the differences between the different groups of adherence within each index.

^bP₂₅=25th percentile, P₇₅=75th percentile.

^cCalculated as weight in kilograms divided by height in meters squared (kg/m²).

Abbreviations: AICR; American Institute for Cancer Research, BMI; body mass index, DBP; diastolic blood pressure, NFBDG; the Norwegian food-based dietary guidelines, SBP; systolic blood pressure, TAG; triglycerides, TC; total cholesterol, WCRF; World cancer research fund.

5 Discussion

In the current master's thesis, the adherence to the NFBDG diet index, the NFBDG lifestyle index and the WCRF/AICR index was investigated, as well as the adherence to each of the components included in the indices, in a population of CRC patients and a population of healthy individuals with moderately elevated risk of CVD. Differences between the genders within each study population were investigated. Furthermore, we looked into the association between index adherence and clinical outcomes such as BP, plasma lipids (TAG and TC) and BMI in the two populations.

In summary, we found that most participants in both study populations were moderate adherent to each of the indices. There was significantly higher adherence to all indices among women than men in both populations. An exception was found in the adherence to the NFBDG lifestyle index in the VISA population, where most participants had moderate to high adherence, and there was a tendency to higher adherence in women than men. Across the indices, the CRC-NORDIET population and the VISA population showed greatest adherence to the recommendations on whole grains, fish, sugar-sweetened beverages, physical activity and tobacco, and poorest adherence was observed for unsalted nuts, red and processed meat, and foods high in sugar and fat. The CRC-NORDIET population also showed poor adherence to dietary supplement use and alcohol. In both populations, there were several significant differences in the adherence to specific components between men and women.

5.1 Methodological considerations

5.1.1 Assessment of dietary intake and adherence to the indices

Two semi-quantitative FFQs were used to collect dietary data from the participants of the two study populations (77, 85). The NORDIET-FFQ was developed to assess adherence to the NFBDG the past 1-2 months, and has been validated by Henriksen *et al.* (77) in a subgroup of the CRC-NORDIET population. The FFQ showed satisfactory validity overall and was able to estimate intake of the main food groups in the NFBDG and the foods associated with cancer risk, except for whole grain products, red and processed meat and water. Additionally, the estimated intake of unsalted nuts was higher, and low-fat dairy products lower in the FFQ compared to the reference method (i.e. weighed records) (77). The VISA-FFQ was developed

from the NORDIET-FFQ, and has been evaluated in the VISA study by Svendsen *et al.* (85). The results showed acceptable validity in the correlations of milk fat intake and a biomarker (i.e. C15:0), and adequate reproducibility for intake of most items in the VISA-FFQ. Concerning reproducibility for the 18 items altered or added in the development of the VISA-FFQ, only the estimated intake of high-fat cheese, whole-fat milk and use of cholesterol-lowering margarine showed significant differences between the test and retest (85). However, none of these three food items are included in the NFBDG indices or the WCRF/AICR index and the affection on the results is likely to be of little importance for the purposes of this thesis.

There is no "gold standard" or absolute reference method for assessing dietary intake, and none of the available methods are able to measure the true intakes (81). The FFQ has been discussed in its ability to assess dietary intake, thereby questioning the validity of results obtained from studies using FFQ (83, 88, 89). However, the FFQ is still widely applied because of important strengths, such as the ability to range individual intakes (previously described in section 1.2.4) (80, 83). Nevertheless, the method relies greatly on the participant's memory, estimation of portion sizes can be difficult, and if self-administered, misunderstandings can appear, causing omission of particular items, which may cause under or over-reporting and misclassification (80, 83). Even though the NORDIET-FFQ and VISA-FFQ have been validated, it is important to be aware of the general strengths and limitations of FFQs when interpreting the findings.

Misclassification in adherence category

Since dietary intake is prone to incorrect estimation, there is a risk of misclassification regarding adherence category. To our knowledge, misclassification in adherence based on different dietary assessment methods is not well studied. An American study by Procter-Gray *et al.* (90) investigated the degree of misclassification in adherence to an index assessed by FFQ compared to 24-HR (90). They found higher mean adherence in both genders when FFQ was used as assessment tool, hence FFQ tended to underestimate the proportion of the study population classified in low adherence (i.e. unhealthy). In the study, 38 % of men and 31 % of women were classified in the low adherence group by the 24-HR, but not by the FFQ (90). Another study by van Lee *et al.* (91) found the same tendency when comparing the two methods, but concluded that both methods could be used for the assessment of adherence to an index (91). The studies by Procter-Gray *et al.* and Lee *et al.* included correlation analysis

between FFQ and 24-HR, which showed some similarities as the correlations found between the FFQ and weighed records in the validation of the NORDIET-FFQ (77, 90, 91). We note that despite satisfactory correlations, there is a risk of misclassification in our results. Nevertheless, the FFQ is a suitable tool of measuring intakes on a group level and to range individual intakes, which may indicate that it is a suitable tool of measuring adherence to an index.

5.1.2 Operationalization of the NFBDG indices and the WCRF/AICR index

Each of the included components in the NFBDG diet index and the NFBDG lifestyle index were weighed equally, and this should be emphasized. For instance, in the NFBDG diet index, intake of unsalted nuts and vegetables are of equal importance with regards to health outcomes. This may be, but it could also be that the individual components affect health outcomes and risk of disease to a varying degree. Thus, the weighing may be based on the expected impact on health outcomes or risk of disease. However, there is a great challenge in evaluating this and to eventually decide how to weigh the components, which was also highlighted in the paper by Shams-White *et al.* (70). It should be kept in mind that regardless of how the components in an index are weighed, the total score of the index can be investigated in its association to risk of morbidity and mortality.

The weighing of components is done somewhat different in the NFBDG indices compared to the WCRF/AICR index. For instance, the diet in total is given one point in the NFBDG lifestyle index, whereas the WCRF/AICR index includes four dietary components. Hence, the importance of diet is more emphasized in the WCRF/AICR index than in the NFBDG lifestyle index. Also, in comparison of the NFBDG diet index to the WCRF/AICR index, the intake of fruits, vegetables, and whole grains is given one point each in the NFBDG diet index, whereas the intake of fruits, vegetables, beans and fiber in the WCRF/AICR index are summarized in one component. This is also the case for intake of red and processed meat, which is separated into two components in the NFBDG diet index, but combined in one component in the WCRF/AICR index. Additionally, the NFBDG diet index is stricter in its cut-off points for intake of fruits and vegetables, but less strict in cut-off points for intake of processed meat, as compared to the WCRF/AICR index. These differences may affect the observed adherences, and could possibly have an impact on the indices' ability to predict health outcomes.

In this thesis, the WCRF/AICR index was operationalized a bit different from the original operationalization (70). Waist circumference was not included, and fiber intake was replaced with whole grains. UPFs were replaced with foods high in sugar and fat, more specifically cakes, pastries, desserts, chocolates, candy, chips and sugar-rich spreads (77). These foods are included in the definition of UPFs, together with other foods that are typically ready to consume, low in dietary fiber, protein, micronutrients and other bioactive compounds, and high in fat, salt and sugar (e.g. cereals, energy bars, French fries, hot dogs, burgers, nuggets, instant noodles) (92). Furthermore, the cut-off values in the original approach were based on the intake of UPFs in the studied population, while predefined cut-off values were used in the present thesis. Thus, the alternative approach used for the UPF component, may not be comparable to studies using the original approach. However, Shams-White *et al.* emphasize that the components included in the index may be adapted to assess adherence if a study does not include adequate information on the original approach (93), which was done in this thesis.

5.1.3 The role of dietary indices in nutritional research

The different indices are developed to predict different outcomes, for instance, risk of NCDs, high blood pressure or cancer. This also applies to the NFBDG indices and the WCRF/AICR index, as the former is developed for the prevention of chronic diseases, and the WCRF/AICR index for the prevention of cancer (70, 76). The different indices aim to reflect specific dietary or lifestyle patterns shown to be associated with risk of disease, and thereby endorse the complexity of the total diet and lifestyle (54). This represents a strength, because dietary components are likely to have additive or antagonistic effects, referred to as food synergy (45). Further, the approach takes into account that the intakes of many foods highly correlate (46, 54). Effects of single nutrients may be small and undetectable, but it may be possible to observe an effect when intakes of foods are combined in dietary pattern analysis (46). However, this approach could also suppress the effect of a single nutrients' impact on health, such as the role of folic acid in neural tube defect (46). Nevertheless, when investigating dietary and lifestyle factors in relation to chronic diseases (e.g. CVD and CRC), the use of indices could provide a broader insight due to the complexity of the diseases and their background.

5.2 Discussion of results

5.2.1 Study populations

The participants included in the current thesis were recruited from the ongoing CRC-NORDIET study (78) and the completed VISA study (84). Among the participants in the CRC-NORDIET study, mean age was 66 years. This is younger than the general Norwegian population of CRC patients, in which median age at diagnosis is 72 years in men and 74 years in women, and 70 years in both genders for colon and rectum cancer, respectively (94). Previous studies have found that the subjects of lowest attendance rate to studies or health surveys tend to be those in the youngest and oldest age groups (95), which could be the reason for the younger age observed among the CRC-NORDIET participants. In addition to age, there is a tendency to higher attendance rate among women, married or cohabitants, employed, higher educated, those with a healthier lifestyle (including less smoking) and with lower prevalence of common chronic diseases (i.e. diabetes, CVD) than non-participants (95-97). The CRC-NORDIET participants had higher education and smoked less than the general Norwegian adult population (98, 99), but did not differ in gender distribution and marital status (100, 101). The VISA population had a higher education level, a higher rate of female participants, smoked more and differed in marital status compared to the general Norwegian adult population (98-101). The differences observed may be due to selection bias, which may limit the representativeness of the study populations and thereby the generalizability of the findings.

Among men in the CRC-NORDIET population, 53 % were diagnosed with cancer of the colon (C18) and 47 % with cancer of the sigmoideum or rectum (C19 and C20). Among women, the distribution was 66 % and 34 % with cancer of the colon and sigmoideum or rectum, respectively. Compared to the most recently published report on cancer in Norway (17), the distribution in the CRC-NORDIET population differs somewhat from the general Norwegian CRC population in that fewer were diagnosed with colon cancer and more with cancer of the sigmoideum or rectum in both genders. However, more women than men are diagnosed with colon cancer and the opposite for sigmoid/rectum cancer (17), which is similar to the CRC-NORDIET population. The percentage of the CRC-NORDIET population that had a stoma (26 %) was lower than in the general CRC population (44 %). This may be because the number of patients with a stoma was only reported for sigmoid/rectum cancer

patients in Norway, while the 26 % includes both patients with cancer of the colon, sigmoideum and rectum (17).

In the CRC-NORDIET population, 45 % were classified as overweight and 20 % as obese. This is higher than in the general Norwegian adult population, where the prevalence is 21 % and 18 % for overweight and obesity, respectively (99). However, our findings are in line with previous studies of CRC patients (102-105). Body fatness is an established risk factor of CRC (20) and this could likely be an explanation for the higher percentages observed, thus making the CRC-NORDIET population representative for CRC patients. The prevalence of overweight and obesity in the VISA population was 40 % and 19 %, respectively, which is similar to the CRC-NORDIET study and therefore also higher than in the general population in Norway. Increased BMI is a risk factor of CVD, dyslipidemia and high blood glucose (106, 107), thereby increasing the probability to be included in the VISA study.

In the CRC-NORDIET population, median BP and TAG were in line with what is considered to be healthy (108, 109). TC was slightly elevated, however similar to the mean in a Norwegian cohort study conducted in the general population (110). In the VISA population, median BP was considered prehypertensive, median TC, LDL-c and TAG were moderately elevated, while median HDL-c was satisfactory (30, 109). However, BP in the VISA population was in the middle of the most recent investigations in the general Norwegian population (110, 111), in addition to higher HDL-c and TAG (110).

5.2.2 Adherence to the NFBDG indices in the CRC-NORDIET population

The CRC-NORDIET participants showed moderate adherence to the NFBDG indices, with a mean adherence of 45 % in the NFBDG diet index and 57 % in the NFBDG lifestyle index. The current thesis was the first study investigating adherence to the NFBDG indices in any population. Adherence to indices among CRC patients have been studied by others (24, 112-115), but the most commonly used approach is to investigate the adherence in association to overall mortality, cancer-recurrence or disease-free survival, and therefore report risk estimates. The mean adherences or the adherence to specific components of the index are not commonly reported. Van Blarigan *et al.* (24) investigated the adherence to the American Cancer Society guidelines for cancer survivors in a population of CRC patients, and found most participants to have moderate or low adherence (24). Another study by Guinter *et al.* (115) investigated the adherence to the American Cancer Society guidelines and DASH

indices, and found a mean adherence of 48 % in the former, and 60 % in the DASH index (115). These indices are somewhat different from the NFBDG indices. However, the findings of moderate adherence to different indices among CRC patients from other studies, strengthens the reliability of the findings in the present thesis, and thereby the reliability of the NFBDG diet index and the NFBDG lifestyle index.

In the most recently conducted national dietary survey in Norway (i.e. Norkost 3) (116), the percentages of men and women adhering to the quantified NFBDGs (i.e. fruits and berries, vegetables, whole grains, fish and red and processed meat) were reported. Compared to the findings in Norkost 3 among the general Norwegian adult population, men in the CRC-NORDIET population had lower adherence to the recommendations on fruits and berries and vegetables, but higher adherence to whole grains and fish (116). Intake of red and processed meat were reported together in Norkost 3, but were assessed separately in the NFBDG diet index. However, 45 % of the men participating in the survey adhered to the recommendation, while 15 % and 12 % of men in the CRC-NORDIET study were adherent to red and processed meat, respectively. Among women, a lower adherence was observed to the recommendation on fruits and berries, but a higher adherence to vegetables, whole grains and fish. Adherence to red and processed meat was observed in 67 % of the women in Norkost 3, compared to 35 % and 23 % to red and processed meat, respectively, among women in the CRC-NORDIET study (116). Dietary supplement use was also reported, with a smaller part of survey participants using dietary supplements than what was observed among the CRC-NORDIET participants. Results of intake of other foods included in the NFBDG diet index were reported with mean intakes, but not as amount of adherent participants, and comparisons were therefore not applicable.

5.2.3 Adherence to the WCRF/AICR index in the CRC-NORDIET population

Similar to the NFBDG diet index and NFBDG lifestyle index, the CRC-NORDIET participants showed moderate adherence to the WCRF/AICR index with a mean adherence of 3.6 points out of 7 (52 %). This finding is in line with other studies conducted (102, 103, 117). To our knowledge, only one study by van Zutphen *et al.* (103) has investigated the adherence to the same WCRF/AICR index as used in this thesis (i.e. developed by Shams-White *et al.* (70)), in a population of Dutch CRC patients. They found the mean adherence

score to be 3.4 points (49 %), which is very similar to our findings (103). Two other studies by Breedweld-Peters *et al.* (102) and Winkels *et al.* (117) investigated adherence to a self-constructed WCRF/AICR index in populations of CRC patients. The studies included ten and eight of the WCRF/AICR recommendations in the constructed index, respectively. The former found a mean adherence of 51 %, whereas the other found a mean adherence of 60 %, which were similar or higher than the present findings. Breedweld-Peters *et al.* (102) also investigated the adherence to the Dutch Healthy Diet index, which was reported to show similar results as the WCRF/AICR index. Thus, the results from other studies seem to be consistent with the present findings of moderate adherence to the WCRF/AICR index among CRC patients (102, 103, 117). However, it should be noted that the WCRF/AICR indices varied a bit in the components included, which may limit the direct comparability.

There was some discrepancies in the findings in this thesis and in the Dutch study by van Zutphen *et al.* (103) regarding adherence to specific components. The CRC-NORDIET population had low adherence to the recommendation of red and processed meat, and moderate adherence to the recommendations of body weight, fruits, vegetables and whole grains, and alcohol, which was also found among the participants in the Dutch study (103). However, the CRC-NORDIET population showed lower adherence to physical activity and higher adherence to sugar-sweetened beverages than the participants in the study by van Zutphen *et al.* (103).

Compared to the findings by Breedweld-Peters *et al.* (102), the CRC-NORDIET population had similar adherence to the components of body weight, red and processed meat, and fruits, vegetables and whole grains. Additionally, the CRC-NORDIET population had higher adherence to physical activity and sugar-sweetened beverages, as well as lower adherence to the recommendation on alcoholic intake than what was found among the participants in the study by Breedweld-Peters *et al.* (102). In contrast to the findings in this thesis, Winkels *et al.* (117) found high adherence to the recommendation on alcohol among their participants. They also found low adherence to red and processed meat, as in the current master's thesis.

Overall, it seem that the CRC-NORDIET population adhered better to the recommendation on sugar-sweetened beverages than other populations of CRC patients, in addition to lower adherence to the recommendation on alcohol intake. They also seem to have similar adherence to body weight, red and processed meat, and fruits, vegetables and whole grains as other CRC populations (102, 103, 117).

5.2.4 Adherence to the NFBDG indices in the VISA population

The adherence to the NFBDG indices in the VISA population was considered to be moderate, with a mean adherence of 46 % in the NFBDG diet index and 61 % in the NFBDG lifestyle index. Adherence to national dietary recommendations in the general populations of different countries has been investigated (57, 118, 119). In an Australian study, the adherence to a dietary index based on national recommendations was found to be 61 % and 67 % in men and women, respectively (119). In a French study, which included physical activity in the index, mean adherence was found to be 50 % in men and 53 % in women (118). Even though these studies were conducted among the general Australian and French population, it is not unlikely that they were nearby similar in characteristics to the VISA population, thus similar adherence is logical to expect.

In the current thesis, adherence to fruits and berries, vegetables, whole grains, fish and red and processed meat among the VISA population differed from what was found in Norkost 3 (116). Both men and women of the VISA study had considerably lower adherence to the recommendation on fruits and berries than the Norwegian adult population, with 6 % and 9 % adhering in this thesis as compared to 34 % and 41 % in men and women, respectively. In addition, men in the VISA study had similar adherence to vegetables, higher adherence to whole grains and fish and lower adherence to red and processed meat (116). Women had higher adherence to vegetables, whole grains and fish, and lower adherence to red and processed meat (116). More men and women of the VISA study were adherent to the recommendation on physical activity than what was found in the Norkost 3 survey (116).

In a study conducted in Luxemburg, an index was built to measure the participants' adherence to thirteen food- and nutrient-based recommendations (57). Comparing the adherence to the NFBDG diet index in the VISA population with the findings of this study, both men and women of the VISA study had lower adherence to fruit and vegetables and higher adherence to fish, low-fat dairy and whole grains. However, the exact percentage of the population being adherent was not directly comparable due to different definitions of the components (i.e. their index measured servings per day, whereas the NFBDG diet index measured grams per day). Nevertheless, the study highlights the fact that large proportions of the population have dyslipidemia (70 %), hypertension (35 %) or obesity (21 %) (120), possibly making this population more similar to the VISA population.

5.2.5 Adherence to the WCRF/AICR index in the VISA population

We observed a moderate adherence to the WCRF/AICR index among the participants of the VISA study, with a mean score of 3.7 out of 7 points (53 %). The adherence to the WCRF/AICR index was recently investigated in a Spanish cohort of elderly individuals at high CVD risk (75). The study population was similar in age to the VISA participants included in this thesis. In line with the present findings, the study reported a mean score of 3.8 points (54 %) (75). Although the Spanish study investigated adherence to an index, the study did not report the adherences to the specific components in the study population (75). Thus, it was not possible to compare their results with our findings. In agreement with the observed adherence to the WCRF/AICR index in both the VISA population and in the Spanish cohort, most other cohort studies have also reported moderate adherence (72, 121).

Adherence to the components in the WCRF/AICR index in different cohort studies have been reported by others (72, 121). Most participants in the VISA study had high adherence to the recommendations on physical activity and intake of sugar-sweetened beverages, and low adherence to the recommended intake of red and processed meat. Additionally, most participants were moderate adherent to the recommendations on body weight, fruits, vegetables and whole grains, and alcohol. Kaluza et al. (72) investigated the adherence in two Swedish populations, and found similar results in adherence to red and processed meat, body weight, and fruits, vegetables and whole grains. However, most of their participants had moderate adherence to physical activity and sugar-sweetened beverages (72), which was lower than the VISA population. Moreover, in the study by Kaluza et al. (72), a higher percentage of the participants had low adherence to alcohol as compared to the VISA population. Another study by Jankovic et al. (121) summarized findings from several largescale cohort studies in a meta-analysis, and reported the adherence to components in the WCRF/AICR index as inconsistent across the different study populations. For instance, the percentage of participants with high adherence to the recommendation on intake of red and processed meat ranged from 2 % in a Swedish cohort, to 76 % in a Greek cohort (121). Thus, there seem to be large variations in adherence to the specific components in different populations.

5.2.6 Gender differences in adherence to the indices

We observed higher adherence to all indices among women than men in both populations, though the difference was not significant in adherence to the NFBDG lifestyle index in the VISA population. In adherence to specific components of the indices, women in the CRC-NORDIET study showed significantly higher adherence than men to fruits and berries, vegetables, whole grains, red meat, processed meat, sugar-sweetened beverages, body weight and alcohol. Men had significantly higher adherence to low-fat dairy as compared to women. Similar findings were found in the VISA study. Compared to men, women showed significantly higher adherence to vegetables, whole grains, sugar-sweetened beverages and body weight.

The tendency of women showing higher adherence to an index or components of an index than men, are supported in other studies (48, 119). Hu et al. (48) found higher percentages of women than men in the highest quintiles of adherence to the HEI, alternative HEI, alternative Mediterranean diet and DASH indices. Not different from these results, McNaughton et al. (119) found higher mean adherence to an Australian dietary recommendations-index among women than among men. In addition, women showed higher adherence to the components of vegetables and low-fat dairy than men, and men showed higher adherence to fruits than women. However, no differences in adherence to alcohol was observed (119). Another study that investigated adherence to the WCRF/AICR recommendations in the Nurse's Health Study and Health Professionals Follow-up Study, found women to have higher adherence to a healthy weight, energy-dense foods, sugar-sweetened beverages, red meat and processed meat than men. Compared to women, men had higher adherence to physical activity, fruits and vegetable and fiber. No different adherence to alcohol between the genders was found (59). The findings of this thesis and of these two studies are somewhat deviating in which of the genders with the highest adherence to a specific component. However, it seems that women more often show higher adherence to the index in total and that women more often than men show higher adherence to specific components.

5.2.7 Associations between adherence to the indices and clinical factors

Some associations between adherence to the NFBDG diet index, NFBDG lifestyle index or WCRF/AICR index and clinical factors were found in this thesis. No association was found between SBP and any index, in either of the two populations. For DBP, TAG and BMI, some inverse associations were found, and TC was positively associated to the WCRF/AICR index in both populations. In line with some of these findings, others have found inverse associations between adherence to an index and SBP, DBP, TC and TAG. The findings are, however, somewhat inconclusive (118, 122, 123). In a French population, no association between adherence and TC was observed, whereas an inverse association to TAG was observed in men, but not in women (118). An American study investigating the HEI found a significant negative correlation between adherence and TC, but a positive correlation with TAG (123). A third study, using data from the same study as the former, found an inverse relationship between index adherence and SBP, DBP and TC. No associations were observed between index adherence and TAG (122).

Regarding BMI, we did not find any association to adherence to the NFBDG diet index. We did find associations to the NFBDG lifestyle index and WCRF/AICR index, but BMI was an included component to these indices and is thereby likely to be the explanation to the observation. It seems that most studies investigating this association find an inverse relationship, but this is not entirely conclusive (122, 124, 125). Additionally, the groups of high adherence to the NFBDG diet index were of limited size in both study populations, which limits the statistical power and the possibility to observe real differences across the adherence groups.

Factors that could influence our observations of associations between index adherence and the clinical factors are the intake of specific foods known to have an impact on the specific clinical factor (i.e. salt and BP (126)). For instance, participants could have low adherence to the components contributing the most to intake of salt, but depending on the adherence to other components, they could end up with an overall low, moderate or high adherence. Thus, salt intake could be the same in all groups of adherence, hence no association is found. This also stresses the importance of looking at dietary patterns and foods rather than nutrients when it comes to overall health, and risk of morbidity and mortality.

5.3 Strengths and limitations

Strengths of the current master's thesis are the large number of subjects (n=494 and n=381 in the CRC-NORDIET and the VISA studies, respectively) and the investigation of adherence to three different indices in two different study populations. The NFBDG indices aim to predict risk of NCDs, whereas the WCRF/AICR index aims to predict risk of cancer. Thus, measuring adherence to different indices may provide broader information on the participants' dietary and lifestyle patterns in relation to both NCDs and cancer, rather than focusing on one index alone. Moreover, the inclusion of the three indices and two populations could provide valuable insight into how different populations adhere to the NFBDG diet and lifestyle indices and the WCRF/AICR index, and thereby suggest which components of the diet and lifestyle with the largest potential for improvement in these populations. This information could potentially provide a basis for individual counselling, health campaigns targeted towards a given population, or areas to be focused on in intervention studies.

Nevertheless, there are some limitations, which should be kept in mind when interpreting the findings. First, the operationalization of the WCRF/AICR index was done differently from the original approach (70), which may reduce the comparability to other studies in adherence to this index. However, this is commonly done because of the variation in data availability within different studies, and is also encouraged when adequate measures are unavailable (93). Second, we included CRC patients and healthy individuals with moderately elevated risk of CVD in this thesis, but no healthy population was included. This could have provided a basis for interesting and important comparison in adherence to the indices between healthy individuals and populations at risk of disease or with established disease. Another source of uncertainty, is the use of self-reported data regarding dietary and lifestyle habits. It is impossible to avoid measurement errors, which may cause misclassification in the assessment of adherence. However, the FFQ is an appropriate tool for ranging individual intakes, and the FFQs used in both studies showed adequate validity (77, 85). Last, this was a cross-sectional designed thesis, which limits the possibility to draw causal conclusions between adherence to any of the included indices and the clinical factors investigated.

6 Conclusions

The overall objective of the current master's thesis was to investigate the adherence to the NFBDG indices and the WCRF/AICR index in a population of CRC survivors and a population of healthy individuals with moderately elevated risk of CVD. The following conclusions can be drawn from this thesis:

- The CRC-NORDIET population and the VISA population showed similarities in adherence to the NFBDG indices and the WCRF/AICR index. Most participants in both populations were moderate adherent, and only small percentages were in the categories of lowest and highest adherence.
- The CRC-NORDIET population and the VISA population showed highest adherence to whole grains, fish, sugar-sweetened beverages, physical activity and tobacco, and lowest adherence to red and processed meat, foods high in sugar and fat, and unsalted nuts. The CRC-NORDIET population also showed low adherence to dietary supplements and alcohol.
- In both the CRC-NORDIET and the VISA population, women showed significantly higher adherence than men to all indices with the exception of the NFBDG lifestyle index in the VISA population. Additionally, women showed significantly higher adherence than men to several components in both populations, hence the conclusion of differences in adherence between genders in these populations can be drawn.
- We found some significant inverse associations between adherence to an index and DBP, TAG and BMI, as well as positive associations between adherence to an index and TC. Regarding SBP, no significant association was found for any of the indices. The results were inconclusive across the three indices in the two populations, and further studies are needed to be able to draw clear conclusions on these associations.

Overall, the NFBDG indices and the WCRF/AICR index investigated in the current master's thesis could be a practical way to examine how different populations adhere to overall and specific recommendations for prevention of chronic diseases and cancer, and to measure dietary and lifestyle patterns.

7 Future perspectives

The present master's thesis was the first thesis to investigate adherence to the newly developed NFBDG indices, as well as the established WCRF/AICR index, in a population of CRC patients and a population of healthy individuals with moderately elevated risk of CVD. This thesis investigated adherence prior to the interventions performed in the CRC-NORDIET study and the VISA study. How participants of the studies adhere to the recommendations after completing the intervention, as well as associated health outcomes, are interesting subjects for further investigations. The main focus areas in the interventions in the CRC-NORDIET study and the VISA study differ, and it would be interesting to investigate if these areas are reflected in a change in adherence to the specific components regarding the focus areas.

Additionally, the adherence to the NFBDG indices should be investigated in the general population. This could provide valuable information on how the population adheres to the recommendations from the health authorities. The next national dietary survey in Norway (i.e. Norkost 4) is in progress (127), which potentially could be used as a basis to measure adherence to the NFBDG indices. Further, this could provide a basis for comparing different populations such as the CRC-NORDIET population and the VISA population to the general Norwegian population. Moreover, investigations of adherence to the NFBDG indices and the WCRF/AICR index in different populations could potentially reveal which dietary and lifestyle factors that have the largest potential for improvement in the population studied. Individually customized advice on diet and lifestyle are the preferred approach, but the revealing of what most people struggle with could provide a basis for what to focus on initially or in recommendations to the general population.

The determinants of adherence to an index or to a specific component of an index could be subject for further examinations. This was not done in the current thesis, but could provide insight into how factors such as education level, marital status, comorbidities or smoking status can affect or predict adherence to an index or component of an index, as well as risk of health and disease outcomes.

References

- 1. World Health Organization. The top 10 causes of death. 2020 [cited 2021 30.04.]. Available from: <u>https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death</u>.
- 2. World Health Organization. Noncommunicable diseases. 2021 [cited 2021 06.05.]. Available from: <u>https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases</u>.
- 3. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.
- 4. Norwegian Institute of Public Health. Causes of death & Life expectancy. [cited 2021 30.04.]. Available from: <u>https://www.fhi.no/en/hn/cause-of-death-and-life-expectancy/#:~:text=The%20main%20causes%20of%20death%20in,Norway%20are%20cardiovascular%20diseases%20and%20cancer.</u>
- 5. World Health Organization. The Global Health Observatory. Global health estimates: Leading causes of DALYs. [cited 2021 07.05.]. Available from: <u>https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/global-health-estimates-leading-causes-of-dalys</u>.
- 6. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1223-49.
- 7. World Health Organization. Tobacco. 2020 [cited 2021 26.04.]. Available from: https://www.who.int/news-room/fact-sheets/detail/tobacco.
- 8. Fernández-Solà J. Cardiovascular risks and benefits of moderate and heavy alcohol consumption. Nat Rev Cardiol. 2015;12(10):576-87.
- 9. Dietary Guidelines Advisory Committee. Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and Secretary of Health and Human Services. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC; 2020.
- 10. Health effects of dietary risks in 195 countries, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2019;393(10184):1958-72.
- 11. Solans M, Chan DSM, Mitrou P, Norat T, Romaguera D. A systematic review and meta-analysis of the 2007 WCRF/AICR score in relation to cancer-related health outcomes. Ann Oncol. 2020;31(3):352-68.
- 12. World Health Organization. Cancer. [cited 2021 06.05.]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer.
- World Cancer Research Fund/American Institue for Cancer Research. Continous Update Project Expert Report. Diet, nutrition, physical activity and colorectal cancer. 2018.
- World Health Organization. Cardiovascular Diseases (CVDs). 2017 [cited 2021 30.04.]. Available from: <u>https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds</u>).
- 15. World Health Organization. International Agency for Research on Cancer. Colorectal cancer. 2020 [cited 2021 24.02.]. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/10 8 9-Colorectum-fact-sheet.pdf.
- 16. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. Nat Rev Gastroenterol Hepatol. 2019;16(12):713-32.

- 17. Cancer in Norway 2019 Cancer incidence, mortality, survival and prevalence in Norway. Oslo: Cancer Registry of Norway; 2020.
- 18. Weinberg BA, Marshall JL, Salem ME. The Growing Challenge of Young Adults With Colorectal Cancer. Oncology (Williston Park). 2017;31(5):381-9.
- 19. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Continuous Update Project 2018.
- 20. World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. Recommendations and public health and policy implications.
- 21. Mehra K, Berkowitz A, Sanft T. Diet, Physical Activity, and Body Weight in Cancer Survivorship. Med Clin North Am. 2017;101(6):1151-65.
- 22. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. Ann Oncol. 2014;25(7):1293-311.
- Balhareth A, Aldossary MY, McNamara D. Impact of physical activity and diet on colorectal cancer survivors' quality of life: a systematic review. World J Surg Oncol. 2019;17(1):153.
- 24. Van Blarigan EL, Fuchs CS, Niedzwiecki D, Zhang S, Saltz LB, Mayer RJ, et al. Association of Survival With Adherence to the American Cancer Society Nutrition and Physical Activity Guidelines for Cancer Survivors After Colon Cancer Diagnosis: The CALGB 89803/Alliance Trial. JAMA Oncol. 2018;4(6):783-90.
- 25. Van Blarigan EL, Meyerhardt JA. Role of physical activity and diet after colorectal cancer diagnosis. J Clin Oncol. 2015;33(16):1825-34.
- 26. Meyerhardt JA, Giovannucci EL, Holmes MD, Chan AT, Chan JA, Colditz GA, et al. Physical activity and survival after colorectal cancer diagnosis. J Clin Oncol. 2006;24(22):3527-34.
- 27. Edwards BK, Noone AM, Mariotto AB, Simard EP, Boscoe FP, Henley SJ, et al. Annual Report to the Nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. Cancer. 2014;120(9):1290-314.
- 28. Jørgensen TL, Hallas J, Friis S, Herrstedt J. Comorbidity in elderly cancer patients in relation to overall and cancer-specific mortality. Br J Cancer. 2012;106(7):1353-60.
- 29. Parés-Badell O, Banqué M, Macià F, Castells X, Sala M. Impact of comorbidity on survival by tumour location: Breast, colorectal and lung cancer (2000-2014). Cancer Epidemiol. 2017;49:66-74.
- 30. Modern Nutrition in Health and Disease. 11th ed: Lippincott Williams & Wilkins, a Wolters Kluwer business; 2014.
- 31. Torres N, Guevara-Cruz M, Velázquez-Villegas LA, Tovar AR. Nutrition and Atherosclerosis. Arch Med Res. 2015;46(5):408-26.
- 32. Norwegian Institute of Public Health. Cardiovascular disease in Norway. 2009. [updated 24.01.2020; cited 2021 30.04.]. Available from: https://www.fhi.no/en/op/hin/health-disease/cardiovascular-disease-in-norway---/.
- 33. Buddeke J, Bots ML, van Dis I, Visseren FL, Hollander M, Schellevis FG, et al. Comorbidity in patients with cardiovascular disease in primary care: a cohort study with routine healthcare data. Br J Gen Pract. 2019;69(683):e398-e406.
- 34. Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts. N Engl J Med. 2018;378(25):e34.

- 35. Sanches Machado d'Almeida K, Ronchi Spillere S, Zuchinali P, Corrêa Souza G. Mediterranean Diet and Other Dietary Patterns in Primary Prevention of Heart Failure and Changes in Cardiac Function Markers: A Systematic Review. Nutrients. 2018;10(1).
- 36. Saeed A, Kampangkaew J, Nambi V. Prevention of Cardiovascular Disease in Women. Methodist Debakey Cardiovasc J. 2017;13(4):185-92.
- 37. Morrissey K. Comorbidity and healthcare use for individuals with CVD in the Ireland: a cross-sectional, population-based study. BMJ Open. 2019;9(1):e025305.
- 38. Kendir C, van den Akker M, Vos R, Metsemakers J. Cardiovascular disease patients have increased risk for comorbidity: A cross-sectional study in the Netherlands. Eur J Gen Pract. 2018;24(1):45-50.
- Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med. 2001;344(1):3-10.
- 40. Vogt TM, Appel LJ, Obarzanek E, Moore TJ, Vollmer WM, Svetkey LP, et al. Dietary Approaches to Stop Hypertension: rationale, design, and methods. DASH Collaborative Research Group. J Am Diet Assoc. 1999;99(8 Suppl):S12-8.
- 41. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004;364(9438):937-52.
- 42. Hjermann I, Velve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease. Report from the Oslo Study Group of a randomised trial in healthy men. Lancet. 1981;2(8259):1303-10.
- 43. Miettinen M, Turpeinen O, Karvonen MJ, Pekkarinen M, Paavilainen E, Elosuo R. Dietary prevention of coronary heart disease in women: the Finnish mental hospital study. Int J Epidemiol. 1983;12(1):17-25.
- 44. Kant AK. Dietary patterns and health outcomes. J Am Diet Assoc. 2004;104(4):615-35.
- 45. Jacobs DR, Jr., Steffen LM. Nutrients, foods, and dietary patterns as exposures in research: a framework for food synergy. Am J Clin Nutr. 2003;78(3 Suppl):508s-13s.
- 46. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002;13(1):3-9.
- 47. Hébert JR, Shivappa N, Wirth MD, Hussey JR, Hurley TG. Perspective: The Dietary Inflammatory Index (DII)-Lessons Learned, Improvements Made, and Future Directions. Adv Nutr. 2019;10(2):185-95.
- 48. Hu EA, Steffen LM, Coresh J, Appel LJ, Rebholz CM. Adherence to the Healthy Eating Index-2015 and Other Dietary Patterns May Reduce Risk of Cardiovascular Disease, Cardiovascular Mortality, and All-Cause Mortality. J Nutr. 2020;150(2):312-21.
- 49. Turati F, Bravi F, Di Maso M, Bosetti C, Polesel J, Serraino D, et al. Adherence to the World Cancer Research Fund/American Institute for Cancer Research recommendations and colorectal cancer risk. Eur J Cancer. 2017;85:86-94.
- Tseng M, Vierkant RA, Kushi LH, Sellers TA, Vachon CM. Dietary patterns and breast density in the Minnesota Breast Cancer Family Study. Cancer Causes Control. 2008;19(5):481-9.
- 51. Kyrø C, Skeie G, Loft S, Overvad K, Christensen J, Tjønneland A, et al. Adherence to a healthy Nordic food index is associated with a lower incidence of colorectal cancer in women: the Diet, Cancer and Health cohort study. Br J Nutr. 2013;109(5):920-7.
- 52. Steck SE, Murphy EA. Dietary patterns and cancer risk. Nat Rev Cancer. 2020;20(2):125-38.

- 53. Nettleton JA, Schulze MB, Jiang R, Jenny NS, Burke GL, Jacobs DR, Jr. A prioridefined dietary patterns and markers of cardiovascular disease risk in the Multi-Ethnic Study of Atherosclerosis (MESA). Am J Clin Nutr. 2008;88(1):185-94.
- 54. Reedy J, Subar AF, George SM, Krebs-Smith SM. Extending Methods in Dietary Patterns Research. Nutrients. 2018;10(5).
- 55. Liese AD, Krebs-Smith SM, Subar AF, George SM, Harmon BE, Neuhouser ML, et al. The Dietary Patterns Methods Project: synthesis of findings across cohorts and relevance to dietary guidance. J Nutr. 2015;145(3):393-402.
- 56. Mazzocchi M, Brasili C, Sandri E. Trends in dietary patterns and compliance with World Health Organization recommendations: a cross-country analysis. Public Health Nutr. 2008;11(5):535-40.
- 57. Alkerwi A, Sauvageot N, Nau A, Lair ML, Donneau AF, Albert A, et al. Population compliance with national dietary recommendations and its determinants: findings from the ORISCAV-LUX study. Br J Nutr. 2012;108(11):2083-92.
- 58. Martínez-González MA, Sánchez-Villegas A. Food patterns and the prevention of depression. Proc Nutr Soc. 2016;75(2):139-46.
- 59. Tabung FK, Fung TT, Chavarro JE, Smith-Warner SA, Willett WC, Giovannucci EL. Associations between adherence to the World Cancer Research Fund/American Institute for Cancer Research cancer prevention recommendations and biomarkers of inflammation, hormonal, and insulin response. Int J Cancer. 2017;140(4):764-76.
- 60. Grafetstätter M, Pletsch-Borba L, Sookthai D, Karavasiloglou N, Johnson T, Katzke VA, et al. Thrombomodulin and Thrombopoietin, Two Biomarkers of Hemostasis, Are Positively Associated with Adherence to the World Cancer Research Fund/American Institute for Cancer Research Recommendations for Cancer Prevention in a Population-Based Cross-Sectional Study. Nutrients. 2019;11(9).
- Jannasch F, Kröger J, Schulze MB. Dietary Patterns and Type 2 Diabetes: A Systematic Literature Review and Meta-Analysis of Prospective Studies. J Nutr. 2017;147(6):1174-82.
- 62. Reedy J, Krebs-Smith SM, Miller PE, Liese AD, Kahle LL, Park Y, et al. Higher diet quality is associated with decreased risk of all-cause, cardiovascular disease, and cancer mortality among older adults. J Nutr. 2014;144(6):881-9.
- 63. Olsen A, Egeberg R, Halkjær J, Christensen J, Overvad K, Tjønneland A. Healthy aspects of the Nordic diet are related to lower total mortality. J Nutr. 2011;141(4):639-44.
- 64. Tertsunen HM, Hantunen S, Tuomainen TP, Salonen JT, Virtanen JK. A Healthy Nordic diet score and risk of incident coronary heart disease among men: the Kuopio Ischaemic Heart Disease Risk Factor Study. Br J Nutr. 2021:1-23.
- 65. Ndanuko RN, Tapsell LC, Charlton KE, Neale EP, Batterham MJ. Dietary Patterns and Blood Pressure in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Adv Nutr. 2016;7(1):76-89.
- 66. Vitale M, Masulli M, Calabrese I, Rivellese AA, Bonora E, Signorini S, et al. Impact of a Mediterranean Dietary Pattern and Its Components on Cardiovascular Risk Factors, Glucose Control, and Body Weight in People with Type 2 Diabetes: A Real-Life Study. Nutrients. 2018;10(8).
- 67. Petimar J, Smith-Warner SA, Rosner B, Chan AT, Giovannucci EL, Tabung FK. Adherence to the World Cancer Research Fund/American Institute for Cancer Research 2018 Recommendations for Cancer Prevention and Risk of Colorectal Cancer. Cancer Epidemiol Biomarkers Prev. 2019;28(9):1469-79.

- 68. Turati F, Dalmartello M, Bravi F, Serraino D, Augustin L, Giacosa A, et al. Adherence to the World Cancer Research Fund/American Institute for Cancer Research Recommendations and the Risk of Breast Cancer. Nutrients. 2020;12(3).
- 69. Romaguera D, Vergnaud AC, Peeters PH, van Gils CH, Chan DS, Ferrari P, et al. Is concordance with World Cancer Research Fund/American Institute for Cancer Research guidelines for cancer prevention related to subsequent risk of cancer? Results from the EPIC study. Am J Clin Nutr. 2012;96(1):150-63.
- Shams-White MM, Brockton NT, Mitrou P, Romaguera D, Brown S, Bender A, et al. Operationalizing the 2018 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Cancer Prevention Recommendations: A Standardized Scoring System. Nutrients. 2019;11(7).
- 71. Barrios-Rodríguez R, Toledo E, Martinez-Gonzalez MA, Aguilera-Buenosvinos I, Romanos-Nanclares A, Jiménez-Moleón JJ. Adherence to the 2018 World Cancer Research Fund/American Institute for Cancer Research Recommendations and Breast Cancer in the SUN Project. Nutrients. 2020;12(7).
- 72. Kaluza J, Harris HR, Håkansson N, Wolk A. Adherence to the WCRF/AICR 2018 recommendations for cancer prevention and risk of cancer: prospective cohort studies of men and women. Br J Cancer. 2020;122(10):1562-70.
- 73. Olmedo-Requena R, Lozano-Lorca M, Salcedo-Bellido I, Jiménez-Pacheco A, Vázquez-Alonso F, García-Caballos M, et al. Compliance with the 2018 World Cancer Research Fund/American Institute for Cancer Research Cancer Prevention Recommendations and Prostate Cancer. Nutrients. 2020;12(3).
- 74. Zhang ZQ, Li QJ, Hao FB, Wu YQ, Liu S, Zhong GC. Adherence to the 2018 World Cancer Research Fund/American Institute for Cancer Research cancer prevention recommendations and pancreatic cancer incidence and mortality: A prospective cohort study. Cancer Med. 2020;9(18):6843-53.
- 75. Barrubés L, Babio N, Hernández-Alonso P, Toledo E, Ramírez Sabio JB, Estruch R, et al. Association between the 2018 WCRF/AICR and the Low-Risk Lifestyle Scores with Colorectal Cancer Risk in the Predimed Study. J Clin Med. 2020;9(4).
- 76. Nasjonalt råd for ernæring. Kostråd for å fremme folkehelsen og forebygge kroniske sykdommer.: Helsedirektoratet; 2011.
- 77. Henriksen HB, Carlsen MH, Paur I, Berntsen S, Bøhn SK, Skjetne AJ, et al. Relative validity of a short food frequency questionnaire assessing adherence to the Norwegian dietary guidelines among colorectal cancer patients. Food Nutr Res. 2018;62.
- 78. Henriksen HB, Ræder H, Bøhn SK, Paur I, Kværner AS, Billington S, et al. The Norwegian dietary guidelines and colorectal cancer survival (CRC-NORDIET) study: a food-based multicentre randomized controlled trial. BMC Cancer. 2017;17(1):83.
- 79. Aune D, Sen A, Prasad M, Norat T, Janszky I, Tonstad S, et al. BMI and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. Bmj. 2016;353:i2156.
- 80. Willett W. Nutritional Epidemiology. 3rd ed: Oxford: Oxford University Press; 2012.
- 81. Margetts BM, Nelson M. Design concepts in nutritional epidemiology. 2nd ed. Oxford: Oxford University Press; 1997.
- 82. Cade J, Thompson R, Burley V, Warm D. Development, validation and utilisation of food-frequency questionnaires a review. Public Health Nutr. 2002;5(4):567-87.
- 83. FAO. Dietary Assessment: A resource guide to method selection and application in low resource settings. Rome; 2018.
- 84. Svendsen K, Telle-Hansen VH, Mørch-Reiersen LT, Garstad KW, Thyholt K, Granlund L, et al. A randomized controlled trial in Norwegian pharmacies on effects of risk alert and advice in people with elevated cardiovascular risk. Prev Med Rep. 2018;12:79-86.

- 85. Svendsen K, Henriksen HB, Østengen B, Jacobs DR, Jr., Telle-Hansen VH, Carlsen MH, et al. Evaluation of a short Food Frequency Questionnaire to assess cardiovascular disease-related diet and lifestyle factors. Food Nutr Res. 2018;62.
- 86. Monteiro CA, Cannon G, Levy R, Moubarac JC, Jaime PC, Martins AP, et al. NOVA. The star shines bright. World Nutr. 2016;7.
- 87. World Health Organization. Body mass index BMI. [cited 2021 24.04.]. Available from: <u>https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi</u>.
- 88. Kipnis V, Midthune D, Freedman L, Bingham S, Day NE, Riboli E, et al. Bias in dietary-report instruments and its implications for nutritional epidemiology. Public Health Nutr. 2002;5(6a):915-23.
- 89. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? Cancer Epidemiol Biomarkers Prev. 2005;14(12):2826-8.
- 90. Procter-Gray E, Olendzki B, Kane K, Churchill L, Hayes RB, Aguirre A, et al. Comparison of Dietary Quality Assessment Using Food Frequency Questionnaire and 24-hour-recalls in Older Men and Women. AIMS Public Health. 2017;4(4):326-46.
- 91. van Lee L, Feskens EJ, Hooft van Huysduynen EJ, de Vries JH, van 't Veer P, Geelen A. The Dutch Healthy Diet index as assessed by 24 h recalls and FFQ: associations with biomarkers from a cross-sectional study. J Nutr Sci. 2013;2:e40.
- 92. Monteiro CA, Cannon G, Moubarac JC, Levy RB, Louzada MLC, Jaime PC. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. Public Health Nutr. 2018;21(1):5-17.
- 93. Shams-White MM, Romaguera D, Mitrou P, Reedy J, Bender A, Brockton NT. Further Guidance in Implementing the Standardized 2018 World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) Score. Cancer Epidemiol Biomarkers Prev. 2020;29(5):889-94.
- 94. Kreftregisteret. Nasjonalt register for tykk- og endetarmskreft, Årsrapport 2019. 2020.
- 95. Eggen AE, Mathiesen EB, Wilsgaard T, Jacobsen BK, Njølstad I. The sixth survey of the Tromso Study (Tromso 6) in 2007-08: collaborative research in the interface between clinical medicine and epidemiology: study objectives, design, data collection procedures, and attendance in a multipurpose population-based health survey. Scand J Public Health. 2013;41(1):65-80.
- 96. Korkeila K, Suominen S, Ahvenainen J, Ojanlatva A, Rautava P, Helenius H, et al. Non-response and related factors in a nation-wide health survey. Eur J Epidemiol. 2001;17(11):991-9.
- 97. Langhammer A, Krokstad S, Romundstad P, Heggland J, Holmen J. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. BMC Med Res Methodol. 2012;12:143.
- 98. Statistics Norway. Educational attainment of the population. 2020 [cited 2021 21.04.]. Available from: <u>https://www.ssb.no/en/utdanning/statistikker/utniv</u>.
- 99. Statistics Norway. Health, care and social relations, survey on living conditions. 2020 [cited 2021 21.04.]. Available from: https://www.ssb.no/en/helse/statistikker/helseforhold.
- 100. Statistics Norway. Population. 2021 [cited 2021 21.04.]. Available from: https://www.ssb.no/en/befolkning/statistikker/folkemengde.
- 101. Statistics Norway. Cohabitants. 2021 [cited 2021 21.04.]. Available from: https://www.ssb.no/en/statbank/table/06854.

- 102. Breedveld-Peters JJL, Koole JL, Müller-Schulte E, van der Linden BWA, Windhausen C, Bours MJL, et al. Colorectal cancers survivors' adherence to lifestyle recommendations and cross-sectional associations with health-related quality of life. Br J Nutr. 2018;120(2):188-97.
- 103. van Zutphen M, Boshuizen HC, Kok DE, van Baar H, Geijsen A, Wesselink E, et al. Colorectal cancer survivors only marginally change their overall lifestyle in the first 2 years following diagnosis. J Cancer Surviv. 2019;13(6):956-67.
- 104. Rohan EA, Townsend JS, Fairley TL, Stewart SL. Health behaviors and quality of life among colorectal cancer survivors. J Natl Compr Canc Netw. 2015;13(3):297-302.
- 105. Grimmett C, Bridgewater J, Steptoe A, Wardle J. Lifestyle and quality of life in colorectal cancer survivors. Qual Life Res. 2011;20(8):1237-45.
- 106. World Health Organization: Obesity and overweight. 2020 [cited 2021 21.04.]. Available from: <u>https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight</u>.
- 107. Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, et al. An Overview and Update on Obesity and the Obesity Paradox in Cardiovascular Diseases. Prog Cardiovasc Dis. 2018;61(2):142-50.
- 109. Helsedirektoratet. Nasjonal faglig retningslinje for forebygging av hjerte- og karsykdom. 2017 [cited 2021 27.04.]. Available from: <u>https://www.helsedirektoratet.no/retningslinjer/forebygging-av-hjerte-ogkarsykdom/utredning-av-lipidverdiene-ved-primaer-og-sekundaerforebygging-avhjerte-og-karsykdom</u>.
- Holmen J, Holmen TL, Tverdal A, Holmen OL, Sund ER, Midthjell K. Blood pressure changes during 22-year of follow-up in large general population - the HUNT Study, Norway. BMC Cardiovasc Disord. 2016;16:94.
- 111. Hopstock LA, Bønaa KH, Eggen AE, Grimsgaard S, Jacobsen BK, Løchen ML, et al. Longitudinal and Secular Trends in Blood Pressure Among Women and Men in Birth Cohorts Born Between 1905 and 1977: The Tromsø Study 1979 to 2008. Hypertension. 2015;66(3):496-501.
- 112. Ratjen I, Schafmayer C, di Giuseppe R, Waniek S, Plachta-Danielzik S, Koch M, et al. Postdiagnostic Mediterranean and Healthy Nordic Dietary Patterns Are Inversely Associated with All-Cause Mortality in Long-Term Colorectal Cancer Survivors. J Nutr. 2017;147(4):636-44.
- 113. Jacobs S, Harmon BE, Ollberding NJ, Wilkens LR, Monroe KR, Kolonel LN, et al. Among 4 Diet Quality Indexes, Only the Alternate Mediterranean Diet Score Is Associated with Better Colorectal Cancer Survival and Only in African American Women in the Multiethnic Cohort. J Nutr. 2016;146(9):1746-55.
- 114. Hoang T, Kim H, Kim J. Dietary Intake in Association with All-Cause Mortality and Colorectal Cancer Mortality among Colorectal Cancer Survivors: A Systematic Review and Meta-Analysis of Prospective Studies. Cancers (Basel). 2020;12(11).
- 115. Guinter MA, McCullough ML, Gapstur SM, Campbell PT. Associations of Pre- and Postdiagnosis Diet Quality With Risk of Mortality Among Men and Women With Colorectal Cancer. J Clin Oncol. 2018;36(34):Jco1800714.

- 116. Helsedirektoratet. Norkost 3. En landsomfattende kostholdsundersøkelse blant menn og kvinner i Norge i alderen 18-70 år, 2010-11. Oslo; 2012.
- 117. Winkels RM, van Lee L, Beijer S, Bours MJ, van Duijnhoven FJ, Geelen A, et al. Adherence to the World Cancer Research Fund/American Institute for Cancer Research lifestyle recommendations in colorectal cancer survivors: results of the PROFILES registry. Cancer Med. 2016;5(9):2587-95.
- 118. Estaquio C, Kesse-Guyot E, Deschamps V, Bertrais S, Dauchet L, Galan P, et al. Adherence to the French Programme National Nutrition Santé Guideline Score is associated with better nutrient intake and nutritional status. J Am Diet Assoc. 2009;109(6):1031-41.
- McNaughton SA, Ball K, Crawford D, Mishra GD. An index of diet and eating patterns is a valid measure of diet quality in an Australian population. J Nutr. 2008;138(1):86-93.
- 120. Alkerwi A, Sauvageot N, Donneau AF, Lair ML, Couffignal S, Beissel J, et al. First nationwide survey on cardiovascular risk factors in Grand-Duchy of Luxembourg (ORISCAV-LUX). BMC Public Health. 2010;10:468.
- 121. Jankovic N, Geelen A, Winkels RM, Mwungura B, Fedirko V, Jenab M, et al. Adherence to the WCRF/AICR Dietary Recommendations for Cancer Prevention and Risk of Cancer in Elderly from Europe and the United States: A Meta-Analysis within the CHANCES Project. Cancer Epidemiol Biomarkers Prev. 2017;26(1):136-44.
- 122. Kant AK, Graubard BI. A comparison of three dietary pattern indexes for predicting biomarkers of diet and disease. J Am Coll Nutr. 2005;24(4):294-303.
- 123. Weinstein SJ, Vogt TM, Gerrior SA. Healthy Eating Index scores are associated with blood nutrient concentrations in the third National Health And Nutrition Examination Survey. J Am Diet Assoc. 2004;104(4):576-84.
- 124. Hsiao PY, Jensen GL, Hartman TJ, Mitchell DC, Nickols-Richardson SM, Coffman DL. Food intake patterns and body mass index in older adults: a review of the epidemiological evidence. J Nutr Gerontol Geriatr. 2011;30(3):204-24.
- 125. Togo P, Osler M, Sørensen TI, Heitmann BL. Food intake patterns and body mass index in observational studies. Int J Obes Relat Metab Disord. 2001;25(12):1741-51.
- 126. Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. Am J Clin Nutr. 2016;103(2):341-7.
- 127. Norkost 4. 2020 [cited 2021 27.04.]. Available from: https://www.med.uio.no/imb/english/research/projects/norkost/index.html.

Supplementary files 1-6

Supplementary file 1: The NORDIET-FFQ



Typisk Norsk-studien

SPØRRESKJEMA OM DE SISTE UKENES KOSTHOLD OG FYSISK AKTIVITET

Vi ønsker opplysninger om ditt vanlige kosthold du har hatt de siste 1-2 måneder.

Skjemaet skal leses av en maskin og det er derfor viktig at du setter tydelige kryss i rutene. Bruk blå eller sort kulepenn. Alle svar vil behandles fortrolig.

Riktig markering i rutene er slik: |X|Ved feil markering, fyll hele ruten slik:



Av hensyn til den maskinelle lesningen - pass på at arkene ikke brettes. Har du spørsmål angående utfyllingen av skjemaet kan du ringe: Hege Berg Henriksen på prosjekttelefon: 932 00 727

Fornavn, mellomnavn:

Etternavn: ____

1. GENERELLE OPPLYSNINGER

Mann	Kvinne		1	- (7	[
Kjønn 🗌		Alder	år	Høyde	cm	Vekt:	kg

2. FRUKT OG BÆR

	Hvo	r mar	nge ga	ange	r <mark>pr.</mark> (du	Hvor mye spiste du pr.gang						
	0	1	2	3	4	5	6-7	8+					
Stor frukt (f.eks. et helt eple, nektarin banan, appelsin, en skive melon o.l.)	ו,								(stk)	1/2		2	3+
Mellomstor frukt (f.eks. klementiner, kiwi, plommer o.l.)									(stk)	1/2	1	2	3+
Liten frukt (f.eks druer o.l.)									(stk)	1-10	11-20	21-40	41+
Bær (ferske og frosne jordbær, blåbæ bringebær, tyttebær, kirsebær o.l.)	r,								(dl)	1/2		2	3+
Tørket frukt (f.eks. rosiner, aprikos, svisker, epler, ferdige blandinger									(dl)	1/2		2	3+

3. NØTTER

	Hvo	r mai	nge g	angei	r pr. ı	du	Hvor mye spiste du pr.gang					
	0	1	2	3	4	5	6-7	8+				
Usaltede nøtter (f.eks. mandler, peanøtter, valnøtter, cashew, ferdig blandinger o.l.)									(neve= 25g)	1/2 1 2 3+		
Saltede nøtter (f.eks. peanøtter, valnøtter, ferdige blandinger, chilinøtter, pekannøtter, mandler o.l.))								(neve= 25g)	1/2 1 2 3+		



V3/V4

4. GRØNNSAKER (ikke potet)

	Hv 0	or ma 1	ange 2	gange 3	er pr.	uke	spiste		Hvor mye spiste du pr.ga	ng
Hvitløk (friske, hermetiske)			2	3	4	5	6-7	8+	(fedd=båt) 1/4 1/2 1 2	3+
Løk, vårløk og purre		 П							(ss) 1 2 3 4	
Tomat (friske, 6 cherry= 1 vanlig									(stk) 1/2 1 2 3	
tomat) Tomatsaus (inkludert ketchup,						·····			(dl)	3+
tomatpure)									(liten 1/4 1/2 1 2	3+
Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.)									bolle=100g)	
Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l)									(dl) 1 2 3 4	5+
5. KORN	Live							d	U	
	пvо 0	r mai 1	nge g 2	jangei 3	грг. (4	uke s 5	piste (6-7	au 8+	Hvor mye spiste du pr. g	ing
Søtet frokostblanding (f.eks.Corn Flakes, Chocofrokost o.l.)		-	_						1/2 1 2 (dl)	3+
Usøtet frokostblanding eller										3+
grøt (f.eks. havregrøt, 4-Korn o.l.)										<u> </u>
6. DRIKKE	Hvor	man	ao a:	angor	nr u	ko dr	akk d		U	
	0	1	2 ye ya	3	4	5	6-7	u 8+	Hvor mye drakk du pr.gai	ıg
Vann (springvann, flaskevann)									(glass) 1/2 1 2 3-4 5-6	7+
Annen drikke uten tilsatt sukker (f.eks. farris, lettsaft, lettbrus o.l.)					. <u></u> .			; <u></u> - !	1/2 1 2 3-4 5-6 (glass)	_ <u></u> 7+
Juice (f.eks. eplejuice, appelsinjuice,	 		·		·				(glass) 1/2 1 2 3-4 5-6	 7+
Manajuice o.l.) Annen drikke tilsatt sukker			·		·				<u>1/2 1 2 3-4 5-6</u>	_ <u>[_]</u> 7+
(f.eks. brus, saft, nektar o.l.)					·			; 	(glass)	7+
Lettmelk, ekstra lettmelk, skummet melk o.l.								;	(glass)	
Helmelk, kefir, kulturmelk o.l.									1/2 1 2 3-4 5-6 (glass)	7+
Øl med alkohol									(glass) 1/2 1 2 3-4 5-6	7+
Vin med alkohol									(glass) 1/2 1 2 3-4 5-6	7+
Brennevin									1/2 1 2 3-4 5-6 (glass)	7+
Kaffe (filterkaffe)									1/2 1 2 3-4 5-6 (kopp)	7+
Annen kaffe (f.eks. espresso,presskanne,kapsel o.l.	 ∖□							 	1/2 1 2 3-4 5-6 (kopp)	7+
Te (f.eks. svart, grønn, urtete o.l.)	<u>/</u>							 	1/2 1 2 3-4 5-6 (kopp)	_ <u></u> 7+
7. KAKER, DESSERT,	GO	DTE	RI							╴└═┙
H	/or ma	ange	gang	er pr.	-	_		_	Hvor mye spiste du pr.ga	ng
0 Kaker, hvetebakst, vafler,	1	2	3 7 (; 4 	4	5	6-7	8+	(stk) 1 2 3 4	5+
søt kjeks Dessert (f.eks. is, hermetisk frukt, pudding)										5+
Sjokolade, godteri] [(porsjon 1/4 1/2 1 11/2 =100g)	2+
Potetgull, chips] [(neve) 1-2 3-5 6-8 9-11	
									454	3



8. BRØD (f.eks. 1/2 rundstykke = 1 skive, 1 baguett = 4 skiver, 1 ciabatta = 2 skiver)

Hvor mange skiver spiste du pr. DAG														
	0	1/2	1	2	3	4	5	6	7	8	9	10	11	12+
Fint brød, 0-25% sammalt mel (f.eks. loff, baguetter, fine rundstykker, ciabatta)														
Halvgrovt brød, 25-50% sammalt mel (f.eks. helkornbrød, kneipp, grove rundstykker)														
Grovt brød, 50-75% sammalt mel (f.eks. havrebrød)														
Ekstra grovt brød, 75-100% sammalt mel (f.eks. mørkt rugbrød)														
Fint knekkebrød (f.eks. kavring, frokost knekkebrød)														
Grovt knekkebrød (f.eks. Husmann, Sport, Solruta o.l.)														
Sum skiver pr.dag= Anta	all skiv	ver pr.	uke:_		x	7=		Ta	llet br	ukes	i spør	smål 9	Э.	

(sum skiver pr.dag) 9. REGISTRER PÅLEGGET DU VANLIGVIS SPISER PÅ DISSE SKIVENE I LØPET AV

		ĸ	
_	U		

	Antall skiver pr. UKE											
		0	1	2-3	4-5	6-7	8-12	13-18	19-24	25-30	31+	
Fete oster som pålegg (f.eks. helfe Norvegia, helfet Jarlsberg, brie o.l.)	t											
Magre oster som pålegg (f.eks. let Norvegia, lett Jarlsberg, cottage chee												
Fiskepålegg (f.eks. makrell i tomat, røket/gravet laks, sild o.l.)												
Rødt kjøtt (f.eks. salami, skinke, servelat, leverpostei, roastbiff o.l.)												
Hvitt kjøtt (f.eks. kyllingpålegg, kalkunpålegg, kyllingleverpostei o.l.)												
Pålegg med sukker (f.eks honning, syltetøy, nøttepålegg o.l.)	_											
Grønnsaker og frukt som pålegg (f.eks. paprika, agurk, avokado, banan, eple o.l.)												
10. Hvilken type sm	ıør/n	narg	arin/	/olje	brukte	e du g	oftest	<u>t</u> til:				
NB! Sett ETT kryss på E hver linje	Bruker i	kke		margariı , Vita, Sc	in (Soft oft oliven) (me	dt smør eierismør mykt, Mo	ir,	soya	er (oliver aolje, ra i hjerteg	apsolje,	
Matlaging, steking, baking]		Г]		Γ]	
På brød, baguette, rundstykke]]]	
11. MEIERIPRODUK		or ma	nge g	anger n	or. uke s	niste (du H	vor mye	o enist	e du pr	gang	
	0	1	2		4 5	6-7	8+	701 m.y.	spice	s uu pi.	gang	
Meieriprodukter med høyt fettinnk (f.eks. seterrømme, creme fraiche, yoghurt o.l.)	nold						[] (dl)		/2 1	11/2	2 3+	
Magre meieriprodukter (f.eks. ekst lettrømme, mager kesam, lett yoghur o.l.)							 ¦(dl)) <mark>1/4 1/</mark>	2 1	11/2	2 3+	
							'				4546	

12. FISK TIL MIDDAG/VARM LUNSJ

	Hvor ma 0 1	nge gange 2 3	erpr.uke 45		Hvor mye sı 8+	piste du pr. gang
Fet fisk til middag (f.eks. laks, ørret, sild, kveite o.l.)					$(\text{porsjon} = \frac{\frac{1}{2}}{145g})$	2 3 4 5+
Mager fisk (f.eks. torsk, sei, hys rødspette, breiflabb o.l.)	e,				$(\text{porsjon} = \frac{\frac{1}{2}}{145g}) \qquad \qquad$	2 3 4 5+
Bearbeidet fisk (f.eks.fiskegrateng, fiskepudding, fiskeboller, fiskegryte o.l.)	, 🔲 🔲				$(porsjon = \frac{\frac{1}{2}}{180g})$	2 3 4 5+
13. KJØTT TIL MI						
		nange gan 1 2	iger pr. uk 3 4	-	10 Hvor mye sp 8+	iste du pr.gang
Rent rødt kjøtt (storfe, svin, sau/lam eller geit)					$\square (porsjon 1/2 1 \\ = 150g) \square \square \square$	2 3 4 5+
Bearbeidet rødt kjøtt (f.eks. kjøttdeig, pølser, hamburger, kjøttboller o.l.)					$\square \qquad (porsjon \ \frac{1}{2} \ 1 \\ = 150g) \ \square \ \square$. 2 3 4 5+
Rent hvitt kjøtt (f.eks. kylling, høne, kalkun o.l.)					$\square \begin{array}{ c c } (porsjon & \frac{1}{2} & 1\\ = 150g) & \square \end{array}$	2 3 4 5+
Bearbeidet hvitt kjøtt (f.eks. pølser, kjøttboller, hamburger o.l	.)				$ \begin{array}{c c} \hline & (porsjon & \frac{1}{2} & 1\\ & =150g) & \hline \end{array} $	2 3 4 5+
14. RIS OG PAST	4					
		mange gar		-		iste du pr.gang
	t 0	. 2	34	5 6-7		2 3 4+
Polert, hvit ris		L L	L		(dl)	2 3 4+
Upolert, naturris					(dl)	
Vanlig pasta					(dl) 1	
Fullkornspasta					(dl) 1	
15. KOSTTILSKU						
	Hvor mar	nge gange 2	rpr.ukes 34	spiste du 5 6-7	-	k du pr. gang
Tran					1 ts	1 bs 1 ss
Trankapsler, Fiskeoljekapsler, omega-3 tilskudd					(kapsler)	
Vitamin D					(piller) 1	2 3 4+
Multivitamin tilskudd					(piller) 1	2 3 4+
16. DAGLIG FYSI	SK AKTI	VITET(F	Registrer he	ele trening	søkter og vanlig fysisk	aktivitet i dagliglivet
Hvor mange ga	anger pr. u	ke var du	fysisk akt	tiv Hvo	or lenge var du fysis nutter)	
0 Moderat intensitet (f.eks.	12	34	5 6-7		-	
hurtig gange, fysisk aktivitet i arbeid, hardt husarbeid, annen aktivitet der du blir lett andpusten)					5-9 10-15 16-20 21-	-30 31-45 46-60 60+
Høy intensitet (f.eks. jogging, skigåing, hard fysisk aktivitet i arbeid, driver trening/idrett, annen aktivitet der du blir veldig andpusten)					5-9 10-15 16-20 21-	4540
]					

Supplementary file 2: The VISA-FFQ

SPØRRESKJEMA KOSTHOLD OG FYSISK AKTIVITET

Vi ønsker opplysninger om ditt vanlige kosthold for en gjennomsnittlig uke. Ha de siste <u>2 månedene</u> i tankene når du fyller ut.

Skjemaet skal leses av en maskin og det er derfor viktig at du setter tydelige kryss i rutene. Bruk blå eller sort kulepenn. Alle svar vil behandles fortrolig.

Riktig markering i rutene er slik: XVed feil markering, fyll hele ruten slik:



Av hensyn til den maskinelle lesningen - pass på at arkene ikke brettes. Har du spørsmål angående utfyllingen av skjemaet kan du ringe: Karianne Svendsen på prosjekttelefon: 22 85 12 10

ID										Besøk 1
	Hvo 0	r mar 1	nge ga 2	angei 3	r pr. ι 4	ike sp 5	oiste 6-7	du 8+	Hvor mye s	piste du pr.gang
Stor frukt (f.eks. et helt eple, nektari banan, appelsin, en skive melon o.l.)	in, 🗌								1/2 (stk)	1 2 3+
Mellomstor frukt (f.eks. klementiner, kiwi, plommer o.l.)									1/2 (stk)	
2. NØTTER										
	Hvor	man	ge ga	nger	pr. u	ke spi	iste d	lu	Hvor mye s	piste du pr.gang
	0	1	2	3	4	5	6-7	8+		
Usaltede nøtter (f.eks. mandler, peanøtter, valnøtter, cashew, ferdig blandinger o.l.)									(neve= 1/2 25g)	1 2 3+
Saltede nøtter (f.eks. peanøtter, valnøtter, ferdige blandinger, chilinøtter, pekannøtter, mandler o.l.)									(neve= 1/2 25g)	1 2 3+
3. GRØNNSAKER (ikke	pote	et)								
•	-	-	ge ga	nger	pr. ul	ke spi	iste d	lu	Hvor mye s	piste du pr.gang
	0	1	2	3	4	5	6-7	8+		
Hvitløk (friske, hermetiske)		1	2	3	4	5	6-7	8+	(fedd=båt)	
Hvitløk (friske, hermetiske) Løk, vårløk og purre		1 	2	3 	4	5	6-7	8+	(fedd=båt) 1/4 (ss) 1	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
			2	3 	4	5	6-7	8+	(fedd=båt)	
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig			2	3 	4	5	6-7	8+	(fedd=båt) 1 (ss) 1/2	
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat,			2	3 	4 			8+	(fedd=båt) 1 (ss) 1/2 (stk) (liten 1/4	
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.) Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål,			2		4				(fedd=båt) (ss) (stk) (liten 1/4 bolle=100g) (dl) 1	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.) Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l)	0		2		4	 			(fedd=båt) (ss) (stk) (liten 1/4 bolle=100g) (dl) 1	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.) Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l) 4. KORN			2		4				(fedd=båt)	2 3 4 1 2 3 1 2 3 1/2 1 2 1/2 1 2 2 3 4 2 3 4 1/2 1 2 1/2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.) Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l) 4. KORN Søtet frokostblanding (f.eks.Corn Flakes, Chocofrokost o.l.)	0		2		4	 			(fedd=båt)	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$
Løk, vårløk og purre Tomat (friske, 6 cherry= 1 vanlig tomat) Blandet salat (f.eks. bladsalat, paprika, agurk, mais o.l.) Andre grønnsaker (f.eks. gulrot, brokkoli, blomkål,kålrot, hodekål, frosne blandinger o.l) 4. KORN Søtet frokostblanding (f.eks.Corn	0		2		4	 			(fedd=båt)	2 3 4 1 2 3 1 2 3 1/2 1 2 1/2 1 2 2 3 4 2 3 4 1/2 1 2 1/2 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1



5. DRIKKE

	Hvor 0	' mai 1	nge g 2	jange 3	rpr.u 4	ke dra 5	akk du 6-7	। 8+	Hvor	mye	drak	k du p	r.gan	g
Vann (springvann, flaskevann)									glass)	1/2	$\begin{bmatrix} 1 \\ \hline \end{bmatrix}$	2 3-4	5-6	7+
Annen drikke uten tilsatt sukker (f.eks. farris, lettsaft, lettbrus o.l.)									glass)	1/2		2 3-4	5-6	7+
Juice (f.eks. eplejuice, appelsinjuice, Manajuice o.l.)									glass)	1/2		2 3-4	5-6	7+
Annen drikke tilsatt sukker (f.eks. brus, saft, nektar o.l.)									glass)	1/2		2 3-4		7+
Helmelk, kulturmelk, kefir o.l.									glass)	1/2		2 3-4	5-6	7+
Lettmelk, ekstra lettmelk, cultura, biola naturell o.l.									glass)	1/2		2 3-4	5-6	7+
Skummet melk, skummet kulturmelk, biola bærdrikk 0,1 % fett o.l.								¦(glass)	1/2		2 3-4	5-6	7+
Øl med alkohol									glass)	1/2	1	2 3-4	5-6	7+
Vin med alkohol								¦(glass)	1/2		2 3-4		7+
Brennevin									glass)	1/2		2 3-4		7+
Kaffe (filtermalt)									kopp)	1/2		2 3-4	5-6	7+
Annen type kaffe (espresso,presskanne,kapsel, kokmalt_o.l.)								¦(kopp)	1/2		2 3-4	5-6	7+
6. MEIERIPRODUKTER														
	Hvo 0	or ma 1	ange 2		er pr. 4	uke sp 5	oiste d 6-7	lu 8+	Hvo	r my	e spis	ste du	pr. ga	ang
Fete produkter (f.eks. kremfløte, creme fraiche, seterrømme o.l.)									1, (dl) [/4 1	./2 :	1 11/2	2	3+
Halvfete produkter (f.eks. matfløte, lettrømme, yoghurt med sukker, lett creme fraiche o.l)]					1 (dl) [/4 1	/2 1 	1 11/2	2	3+
Magre produkter (f.eks. kaffefløte, ekstra lett rømme, kesam, matyoghur yoghurt naturell/Dobbel 0% o.l)	t 🗌								1 (dl) [_/4 :	1/2 1		2 2	3+
7. BRØD (f.eks. 1/2 rundstykke =	= 1 ski	ve, 1	bague	ett = 4	skiver,	1 ciaba	itta = 2	skive	r)					
	H	vor r	mang	je skiv	ver spi	ste dı	ı pr. D	AG						
Fint brad 0 2E% commolt mol	0) :	1/2	1	2	34	5	6	7	8	9	10	11	12+
Fint brød, 0-25% sammalt mel (f.eks. loff, baguetter, fine rundstykke ciabatta)	er, [
Halvgrovt brød, 25-50% sammalt (f.eks. helkornbrød, kneipp, grove rundstykker)	mel													
Grovt brød, 50-75% sammalt mel (f.eks. havrebrød)]			
Ekstra grovt brød, 75-100% samn mel (f.eks. mørkt rugbrød)	nalt													
Fint knekkebrød (f.eks. kavring, frol knekkebrød)	kost													
Grovt knekkebrød (f.eks. Husmann, Sport, Solruta o.l.)														
Sum skiver pr.dag=		An	tall sl	kiver p				=		. Tal	let bru	ıkes i s	pørsm	nål 8.
					(sum	skiver pi	r.dag)						25070	,



8. REGISTRER PÅLEGGET DU VANLIGVIS SPISER PÅ DISSE SKIVENE I LØPET AV EN UKE:

					Antan	skiver	pr. UK				
		0	1	2-3	4-5	6-7	8-12	13-18	19-24	25-30	31+
Fete oster som pålegg (f.eks. hv nøkkelost, Gudbrandsdalsost, brie											
Halvfete oster som pålegg (f.ek hvitost,lettere Gudbrandsdalsost, k smørbare oster, prim o.l.)	s. lettere ettere										
Andre oster som pålegg (f.eks. gulost, cottage cheese, lettere prin gulost" med 10 % fett o.l.)											
Fete kjøttpålegg (f.eks. salami, s falukorv, vanlig leverpostei o.l.)	servelat,										
Magre kjøttpålegg (f.eks. kokt/r skinke, kylling/kalkunpålegg, lett s mager eller oljebaserte leverpostei	ervelat,										
Pålegg med sukker (f.eks. honni syltetøy, nøttepålegg o.l.)	ing,										
Grønnsaker og frukt som påleg (f.eks. paprika, agurk, avokado, banan, eple o.l.)	g										
Fiskepålegg (f.eks. makrell i tom røket/gravet laks, sild o.l.)	at,										
9. EGG											
	Anta	ll pr. u	uke								
Hvor mange egg, inkludert i matlaging, spiser du pr. uke?											
10. Hvilken type smøi	/marg	jarin	/olje	bruk	cte du	<u>ofte</u>	<u>st</u> til:	1			
NB! Sett ETT kryss på hver linje	Bruker il	ke	Mykt m Flora, \		n (Soft oft oliven	្ញ (m	rdt smø eierism emykt, l		soy	er (olive vaolje, ra a hjerteg	apsolje,
Matlaging, steking, baking]]]
På brød, baguette, rundstykke]]
11. KOLESTEROLSENK		ΜΔΕ	RGARI	[N							
	Nei	,			laglig		Ja,	av og t	il	Ve	et ikke
Bruker du Vita Pro-Aktiv eller Becel Pro-Activ?							•				
12. FISK TIL MIDDAG			NCI								
	/ • АЛР	. LU	1135								

	Hvoi	r man	nger 3			ste du 6-7		Hvor mye spiste du pr. gang
	U	1	 	-	-	• •	8+	
Fet fisk (f.eks. laks, ørret, sild, kveite o.l.)								$\begin{array}{c c c c c c c c c c c c c c c c c c c $
Mager fisk (f.eks. torsk, sei, hyse, rødspette, breiflabb o.l.)								$ (porsjon = \frac{1/2}{1} \ 1 \ 2 \ 3 \ 4 \ 5+ \\ 145g) \ \Box \ $
Bearbeidet fisk (f.eks.fiskegrateng, fiskepudding, fiskeboller, fiskegryte o.l.)								$\begin{array}{c ccccccccccccccccccccccccccccccccccc$



13. KJØTT TIL MID	DAG		RM I	LUN	SJ										
	Ηνοι	r <mark>mar</mark>	nge ga	anger	pr. u	ike sp	oiste (du	Hvor r	nye	spis	te dı	ı pr.	gang	
	0	1	2	3	4	5	6-7	8+	1						
Fete kjøttprodukter (f.eks. familiedeig, vanlig grillpølser/wienerpølser, stek med fettrand, bacon, flesk o.l.)									(porsjon =150g)	¹ /2		2	3	4	5+
Halvfete kjøttprodukter (f.eks. kjøttdeig (okse,lam), kyllingpølse, lettpølse, hamburger, kylling med skinn o.l)									(porsjon =150g)	1/2	1	2	3	4	5+
Magre kjøttprodukter (f.eks. karbonadedeig, kjøttdeig (svin,kylling biff, filet (kylling, svin, okse, lam), viltkjøtt, "Go' og mager pølser" o.l.)), 								(porsjon =150g)	1/2	1	2	3	4	5+
14. RIS OG PASTA															

Hvor mange ganger pr. uke spiste du Hvor mye spiste du pr.gang 0 2 3 5 6-7 8+ 1 4 2 3 4+ (dl) Polert, hvit ris 2 3 4+ 1 Upolert, naturris (dl) _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ 2 3 1 4+ Vanlig pasta (dl) $\left[\right]$ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ - -_ 2 3 4+ 1 Fullkornspasta (dl)

15. KAKER, DESSERT, GODTERI

	Hvo 0	or man	nge ga	anger 2	r pr. ul	e spis 5	te du 6-7	Hv 8+	or my	e spis	te du	pr.gar	ng
Kaker, hvetebakst, vafler, søt kjeks								st (st	<)	2	3	4 5	+
Dessert (f.eks. is, hermetisk frukt, pudding)								(dl)		2	3	4 5	+
Sjokolade, godteri								(porsj	on 1/4	1/2			2+
Potetgull, chips								(nev	1-2 e)	3-5	6-8	9-11 1	2+
16. RØYKING													
	I	Nei			J	a, av o	g til		Ja, da	glig			
Røyker du?													
Hvis ja, hvor mange sigaretter/piper røyker du i gjenomsnitt <i>pr. dag</i> ? Antall:													
17. DAGLIG FYSISK	ΑΚΤ	Ινιτ	ET (F	Regist	rer hel	e trenir	ngsøkte	er og vanlig	fysisk	aktivi	tet i da	agligliv	et)
Hvor mange ga 0	anger 1	pr. uk 2	ke var 3	du fy 4	-	ktiv -78+		or lenge va nutter)	r du fy	/sisk a	ıktiv p	or. gan	g
Moderat intensitet (f.eks. hurtig gange, fysisk aktivitet i arbeid, hardt husarbeid, annen aktivitet der du blir lett andpusten)							1-4	5-9 10-15	16-20	21-30	31-45	46-60	60+
Høy intensitet (f.eks. jogging, skigåing, hard fysisk aktivitet i arbeid, driver trening/idrett, annen aktivitet der du blir veldig andpusten)]						5-9 10-15	16-20	21-30	31-45	46-60	60+
	7												



Supplementary file 3: Ethical approval for the CRC-NORDIET study



UNIVERSITETET I OSLO

DET MEDISINSKE FAKULTET

Professor Rune Blomhoff Institutt for medisinske basalfag Universitetet i Oslo Postboks 1046 Blindern 0316 Oslo Regional komité for medisinsk og helsefaglig forskningsetikk sør-øst C (REK sør-øst C) Postboks 1130 Blindern NO-0318 Oslo

Telefon: 22 84 46 67

Dato: 29.04.2011 Deres ref.: Vår ref.: 2011/836 (oppgis ved henvendelse)

E-post: <u>post@helseforskning.etikkom.no</u> Nettadresse: <u>http://helseforskning.etikkom.no</u>

Typisk norsk!

Vi viser til søknad mottatt til frist 22.03.2011 om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden er blitt vurdert av Regional komité for medisinsk og helsefaglig forskningsetikk i henhold til lov av 20. juni 2008 nr. 44, om medisinsk og helsefaglig forskning (helseforskningsloven) kapittel 3, med tilhørende forskrift om organisering av medisinsk og helsefaglig forskning av 1. juli 2009 nr 0955.

Både økt forekomst og overlevelse etter behandling gjør at et økende antall personer lever med en tidligere kreftdiagnose. Disse personene har større sannsynlighet for å utvikle andre livsstilssykdommer enn resten av befolkningen i samme alder. Man ønsker i denne studien å undersøke hvordan et endret kosthold påvirker helsetilstanden og utvikling av livsstilssykdommer etter behandling for tykk- og endetarmskreft. Kostholdet i studien er basert på de nye kostrådene fra Helsedirektoratet og matvarer som i epidemiologiske- og eksperimentelle studier er vist å hemme inflammasjon eller oksidativt stress, og med et fokus på norske matvaner. Kostholdsintervensjonen kombineres med intensiv oppfølging, som er nødvendig for høy compliance til kosten.

Prosjektleder:Rune BlomhoffForskningsansvarlig:Universitetet i Oslo, Medisinsk fakultet

Forskningsetisk vurdering

Komiteen har ingen forskningsetiske innvendinger til studien i seg selv, men mener prosjektleder bør vurdere å oversette og benytte den engelske tittelen *Effect of the new Norwegian food based dietary guidelines on chronic diseases in colorectal cancer survivors,* da denne tittelen oppleves å bedre beskrive formålet med prosjektet. Tittelen skal også endres på informasjonsskrivet.

Det anføres på s. 564 i den vitenskapelige protokollen: *Total genome transcriptomics, low density gene arrays as well as RT-PCR will be performed on white blodd cells (WBC) taken from the participants during visits to the study centre or hospital. Gene expression profiling will also be performed on tissue samples of tumor and neighboring healthy tissues removed during surgery.*

Komiteen bemerker at dersom det skal gjøres helgenomsekvensering i prosjektet, kan man risikere å komme over utilsiktede funn med prediktiv verdi for både pasient og pårørende. Komiteen mistenker at prosjektet kan komme til å falle inn under bestemmelsene i bioteknologiloven, men gjør oppmerksom på at søker selv plikter å avklare dette med Helsedirektoratet ved tvil. Komiteen forutsetter at det finnes beredskap for å håndtere eventuelle uventede funn.

Forskningsbiobank

Det søkes om å opprette en spesifikk forskningsbiobank med navn *The Norwegian Foods Study* i prosjektet.

Ansvarshavende for forskningsbiobanken er Rune Blomhoff. Forskningsansvarlig er Institutt for Medisinske Basalfag, Universitetet i Oslo.

Biobanken vil bestå av blodprøver.

Biobanken planlegges å vare til 2040. Deretter skal materialet behandles i henhold til helseforskningslovens § 30.

Biologisk materiale vil utføres til utlandet i henhold til helseforskningslovens § 29. Deltakerne er orientert om dette i informasjonsskriv.

Informasjonsskriv og samtykkeerklæring

Det anføres i informasjonsskrivet til deltakerne at *studiens målsetning er at du skal forbedre dine kostvaner og at du skal nærme deg kostrådene som utgitt av Helsedirektoratet.* Komiteen oppfatter ikke at dette er formålet med studien. Formålet med studien er å undersøke hvordan et endret kosthold påvirker helsetilstanden og utvikling av livsstilssykdommer etter behandling for tykk- og endetarmskreft. Denne informasjonen må således rettes.

Ut fra dette setter komiteen følgende vilkår for prosjektet:

- 1. Tittel på studien skal endres i informasjonsskrivet, for bedre å reflektere studiens formål.
- 2. Informasjonsskriv skal revideres i tråd med det ovennevnte.

Vedtak:

Prosjektet godkjennes under forutsetning av at ovennevnte vilkår oppfylles.

Komiteen godkjenner opprettelse av forskningsbiobanken *The Norwegian Foods Study*, i tråd med det som er angitt i prosjektsøknaden. Biobankregisteret vil bli underrettet ved kopi av dette brev

I tillegg til vilkår som fremgår av dette vedtaket, er tillatelsen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknaden og protokollen, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2040. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato. Prosjektet skal sende sluttmelding på eget skjema, jf. helseforskningsloven § 12, senest et halvt år etter prosjektslutt.

Komiteens avgjørelse var enstemmig.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for *Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse- og omsorgssektoren:*

http://www.helsedirektoratet.no/samspill/informasjonssikkerhet/norm_for_informasjonssikkerhet_i_helsesektoren_232354

Hvis forskningsbiobanken opphører, nedlegges eller overtas av andre, skal det søkes REK om tillatelse, jf. helseforskningloven § 30.

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. Forvaltningslovens § 28 flg. Eventuell klage sendes til REK sør-øst. Klagefristen er tre uker fra mottak av dette brevet.

Med vennlig hilsen

Arvid Heiberg (sign.) professor dr. med. leder

Tor Even Svanes seniorrådgiver

Kopi: Universitetsdirektøren, universitetsdirektørens kontor, Pb 1072 Blindern, INTERNPOST Biobankregisteret v/ <u>nina.hovland@fhi.no</u>

Vi ber om at alle henvendelser sendes inn via vår saksportal: <u>http://helseforskning.etikkom.no</u> eller på e-post til: <u>post@helseforskning.etikkom.no</u>. Vennligst oppgi vårt saksnummer/referansenummer i korrespondansen.

Supplementary file 4: Ethical approval for the VISA study



Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Gjøril Bergva	22845529	16.12.2013	2013/1660/REK sør-øst D
			Deres dato:	Deres referanse:
			29.10.2013	
			Vår referanse må oppgis v	red alle henvendelser

Til: Kjetil Retterstøl

2013/1660 D Effekt av screening av risikofaktorer for hjerte- og karsykdom i apotek

Vi viser til klage, mottatt 29.10.2013, på komiteens behandling av ovennevnte søknad. Klagen ble behandlet på komiteens møte 27.11.2013.

Forskningsansvarlig: Universitetet i Oslo Prosjektleder: Kjetil Retterstøl

Prosjektomtale

Utgangspunkt for prosjektet er at blodtrykk, kolesterolnivå og blodsukker er viktige risikofaktorer for hjerte og karsykdommer (HKS). I prosjektet skal man gjennomføre en gratis screening med målinger av disse risikofaktorene samt midjemål og vekt i ca. 150 apoteker i landet. Deltakerne skal i tillegg besvare et spørreskjema. Basert på resultatene fra målingene og spørreskjemaet, vil helsepersonell ved apotek regne ut deltakernes individuelle risikoscore. De med høy risiko for HKS, vil bli bedt om å screene seg på nytt etter 8 uker. 10 % av dem som oppsøker apotek vil ikke bli screenet første gang, men bli forespurt om å komme tilbake om 8 uker. Formålet med prosjektet er å vurdere om kunnskap om egen risiko for HKS har effekt på livsstil etter 8 uker og 1 år. Det skal inkluderes 25 000 forskningsdeltakere. Data fra intervensjonsgruppen skal kobles til Norsk pasientregister, Reseptregisteret og Dødsårsaksregisteret etter 2 og 5 år.

Det er tidligere gjennomført en kolesterolkampanje i apotek som la grunnlag for stipendiatens masteroppgave. Prosjektet ble framlagt for REK og ble vurdert til å falle utenfor REKs mandat (2012/517).

Saksgang

Søknaden ble første gang behandlet i møtet 23.09.2013. Komiteen avslo prosjektet med følgende begrunnelse: «Etter komiteens syn er det ikke et rimelig forhold mellom forutsigbar nytte og ulempe for deltagerne. Gevinsten av screeningen er såpass marginal at den ikke berettiger den uro og bekymring deltagelse i prosjektet kan medføre. Komiteen finner ikke at hensynet til deltagernes velferd og integritet er ivaretatt på en tilfredsstillende måte, jfr helseforskningsloven § 5».

Prosjektleders klage ble mottatt 29.10.2013

Klagers anførsler

I klagen viser prosjektleder til at ny styrkeberegning er utført og at antall deltagere er redusert for å bedre ivareta forholdet mellom nytte og ulempe. Nytten for den enkelte vil, ifølge søker, primært bestå i at uoppdaget diabetes, hypertensjon eller hyperkolesterolemi kan avdekkes, og at de vil få livsstilsråd i henhold til retningslinjene. Prosjektleder viser til erfaringer og tidligere studier som viser at deltakere i slike undersøkelser i hovedsak er fornøyde med å bli undersøkt. Det vises også til samfunnsnytten i at prosjektet har en forebyggende karakter. Det er redegjort nærmere for rekrutteringen til studien, behovet for

Besøksadresse: Gullhaugveien 1-3, 0484 Oslo registerkobling er begrunnet og metode for gjennomføring av registerkobling er beskrevet. Søker erkjenner at det er vanskelig å finne egnet kontrollgruppe, men en ny runde i Tromsøundersøkelsen i 2014 vil kunne gi mulighet til å finne matchede kontroller på en rekke parametre.

Komiteens vurdering

Komiteen konstaterer at prosjektleder har gitt et grundig tilsvar, og det er lagt inn en rekke endringer i prosjektets design for å imøtekomme komiteens innvendinger. Etter en helhetlig vurdering har komiteen kommet til at studien, slik den nå er fremlagt, er forsvarlig å gjennomføre.

Komiteen legger merke til at det er diskrepans mellom protokoll og informasjonsskriv når det gjelder registerkobling. Komiteen setter derfor som vilkår for godkjenning at informasjonsskrivene oppdateres i tråd med den reviderte protokollen. Skrivene skal sendes komiteen til orientering.

Vedtak

Komiteen omgjør sitt opprinnelige vedtak, jfr. forvaltningsloven § 33, annet ledd.

Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres under forutsetning av at ovennevnte vilkår oppfylles.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad, klage og revidert protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 31.12.2020. Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 31.12.2025. Forskningsfilen skal oppbevares avidentifisert, dvs. atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren».

Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

Klageadgang

Du kan klage på komiteens vedtak, jf. forvaltningslovens § 28 flg. Klagen sendes til REK sør-øst D. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst D, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Vi ber om at alle henvendelser sendes inn på korrekt skjema via vår saksportal: http://helseforskning.etikkom.no. Dersom det ikke finnes passende skjema kan henvendelsen rettes på e-post til: post@helseforskning.etikkom.no.

Vennligst oppgi vårt referansenummer i korrespondansen.

Med vennlig hilsen,

Finn Wisløff Professor em. dr. med. Leder Kopi til: <u>e.h.mjelde@medisin.uio.no</u>, Universitetet i Oslo

Supplementary file 5: Clinical characteristics of the CRC-NORDIET participants

	Total	Men	Women	p ^a
Days since surgery, mean ± SD	162 ± 60	162 ± 58	162 ± 62	0.95
Stoma, n (%)	129 (26.1)	83 (31.3)	46 (20.1)	0.006
Completed or on-going				0.36
treatment, n (%)				0.50
No-ongoing treatment	193 (87.7)	103 (89.6)	90 (85.7)	
Chemotherapy	26 (11.8)	11 (9.6)	15 (14.3)	
Radiation	1 (0.5)	1 (0.9)	0 (0)	
Tumor localization, n (%)				0.02
C18 Colon	284 (58.8)	137 (52.9)	147 (65.6)	
C19 Rectosigmoid	22 (4.6)	12 (4.6)	10 (4.5)	
C20 Rectum	174 (36.0)	109 (42.1)	65 (29.0)	
C18/C19, C18/C20 ^b	3 (0.6)	1 (0.4)	2 (0.9)	
Tumor classification, n (%)				0.17
TNM stage I	133 (31.1)	80 (36.1)	53 (25.4)	
TNM stage II	161 (36.9)	79 (34.8)	82 (39.2)	
TNM stage III	140 (31.5)	67 (28.8)	73 (34.9)	
TNM stage IV	2 (0.5)	1 (0.4)	1 (0.5)	

Supplementary file 5: Clinical characteristics of the CRC-NORDIET population in total and stratified by gender

^aIndependent samples t-test for continuous variables and chi-square tests for categorical variables, p-values for the differences between men and women. P<0.05 was considered statistically significant (marked in bold). ^bParticipants registered with two localizations.

Abbreviations: CRC-NORDIET; the Norwegian dietary guidelines and colorectal cancer study, TNM; tumor node metastases

Supplementary file 6: Estimated intakes of food groups in the two populations

	Cl	RC-NORDIET	VISA				
	Men	Women	p ^b	Men	Women	p ^b	
Fruits and							
berries ^c	165 (91, 240)	198 (112, 280)	0.001	131 (73, 176)	123 (85, 191)	0.46	
Vegetables	123 (71, 179)	164 (95, 239)	<0.001	120 (79, 209)	166 (106, 269)	0.001	
Whole grains	86 (47, 124)	87 (51, 124)	0.58	89 (51, 135)	90 (58, 129)	0.61	
Unsalted							
nuts	2 (0, 7)	4 (0, 11)	0.05	4 (0, 11)	5 (0, 14)	0.11	
Fish	81 (54, 115)	74 (46, 107)	0.08	75 (50, 111)	77 (53, 116)	0.49	
Low-fat							
dairy	93 (7, 188)	47 (7, 156)	0.05	93 (6, 201)	133 (29, 232)	0.19	
Red meat	65 (46, 92)	46 (25, 70)	<0.001	95 (62, 144)	79 (48, 117)	0.009	
Processed							
meat	45 (25, 68)	27 (13, 48)	<0.001	46 (23, 87)	35 (14, 58)	<0.00	
Foods high in							
sugar and fat	59 (32, 112)	62 (31, 98)	0.88	62 (35, 108)	51 (25, 89)	0.02	
Sugar-							
sweetened							
beverages	0 (0, 58)	0 (0, 28)	0.002	0 (0, 29)	0 (0, 14)	<0.00	
Alcoholic							
drinks	142 (30, 310)	32 (0, 112)	<0.001	105 (0, 253)	32 (0, 104)	<0.00	

Supplementary file 6: Estimated intake of different food groups and drinks in the men and women of the two populations, in grams per day. Presented as medians with percentiles^a

^a25th percentile and 75th percentile. ^bMann-Whitney U test, p-value for the differences in intake between men and women in the CRC-NORDIET study and between men and women in the VISA study. P<0.05 was considered statistically significant (marked in bold).

^cIncludes juice, defined as maximum 1 portion of fruit (=100 g).

Abbreviations: CRC-NORDIET; the Norwegian dietary guidelines and colorectal cancer study, VISA; the Vascular lifestyle-intervention and screening in pharmacies study.